

# STIC Search Report Biotech-Chem Library

## STIC Database Tracking Number: 168212

TO: Tamthom Truong Location: rem/5B19/5C18

Art Unit: 1624

Tuesday, October 18, 2005

Case Serial Number: 10/088854

From: John DiNatale

**Location: Biotech-Chem Library** 

**REM-1B65** 

Phone: (571)272-2557

john.dinatale@uspto.gov

### Search Notes

Examiner Truong,

See attached results.

If you have any questions about this search feel free to contact me at any time.

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John DiNatale Technical Information Specialist STIC Biotech/Chem Library (571)272-2557



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168212





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*Office Location: REM 5B19						
*Phone No.: x 20676						
Mailbox No.: R	EM 5C18					

\*Case serial number: 10/ 088,854

If not related to a patent application, please enter NA here.

Class / Subclass(es) 514/ 266.1 & 544/ 284

Earliest Priority Filing Date: 09-21-1999

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#### Provide detailed information on your search topic:

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10/088,854  $X = 0, S, S(0), S(0)_2, NH or NR^8$ R8 = H. or alkyl R9 = H, ethenyl, opt. sub. phenyl, or gpt. sub. furanyl. opt. sub. pyridyl, or gpt. sub. furanyl.

See also claim 11

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**CONFIRMATION NO. 6749** 

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SERIAL NUMBEI 10/088,854	FILING DATE 03/21/2002 RULE	(	CLASS 514	GROUP A		DC	ATTORNEY OCKET NO. Z70601-1	
APPLICANTS  Andrew Austen Mortlock, Macclesfield, UNITED KINGDOM;  Nicholas John Keen, Macclesfield, UNITED KINGDOM;					It and			
This applicati	** CONTINUING DATA **********************************							
UNITED KINGDOM 9922156.6 09/21/1999 UNITED KINGDOM 9922152.5 09/21/1999 UNITED KINGDOM 9922159.0 09/21/1999								
Foreign Priority claimed 35 USC 119 (a-d) condition met Verified and Acknowledged	yes no yes no Met Allowance Examiner's Signature	et after Initials	STATE OR  COUNTRY UNITED KINGDOM	SHEETS	CLAI	MS	INDEPENDENT CLAIMS 1	
ADDRESS 44992 ASTRAZENECA RA 35 GATEHOUSE D WALTHAM , MA 02451-1215								
TITLE Quinazoline compo	ounds and pharmaceutic	ical composi	itions containin	g them				
FILING FEE FE	EES: Authority has been	en given in Pa					) essing Ext. of	

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RECEIVED No for following:	☐ 1.18 Fees ( Issue )		
	Other		
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Application No. 10/088,354 Amendment Dated 08/12/2005 Reply to Office Action of 03/14/2005

#### Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Listing of Claims:

1-10. (Cancelled)

#### 11. (Currently amended) A compound of formula (IIB)

$$R^{60}$$
 $R^{60}$ 
 $R^{60}$ 

or a sail, ester, amide or produg thereof where

X is O, or S, S(O) or S(O)<sub>2</sub> NH or NR<sup>8</sup> where R<sup>8</sup> is hydrogen or C<sub>1-6</sub>alkyl, Z is O or S.

R° is hydrogen ex-eptionally substituted hydrocarbyl or eptionally substituted heterocyclyl ethenyl, optionally substituted phenyl, optionally substituted pyridyl or optionally substituted furanyl where optional substituents for R³ groups are C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkyl, halo or nitro, R⁵ and R³ are independently selected from hydrogen, halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxymethyl, di(C<sub>1-4</sub>alkoxy)methyl, C<sub>1-4</sub>alkanoyl, trifluoromethyl, cyano, amino, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated and [[([]]linked via a ring carbon or nitrogen atom[[[]]] or unsaturated and [[([]]linked via a ring carbon atoms[[]]], and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C<sub>1-2</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C<sub>2-4</sub>alkanoyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>alkylsulphanyl, C<sub>1-4</sub>alkylsulphinyl, C<sub>1-4</sub>alkylsulphonyl, carbamoyl, N-C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl,

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PAGE 7/22 \* RCVD AT 8/12/2005 5:25:06 PM [Eastern Daylight Time] \* SVR:USPTO-EFXRF-8/0 \* DNIS:8729306 \* CSID:17818394121 \* DURATION (mm-ss):06-52

Application No. 10/088,i354 Amendment Dated 08/12/2005 Reply to Office Action of 03/14/2005

aminosulphonyl, N-C<sub>1-4</sub>alkylarninosulphonyl, N,N-di(C<sub>1-4</sub>alkyl)aminosulphonyl, C<sub>1-4</sub>alkylsulphonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrotidinyl, p perazinyl, piperidinyl, imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkarioyloxy, trifluoromethyl, cyano, amino, nitro and C<sub>1-4</sub>alkoxycarbonyl, R<sup>1</sup> is hydrogen, R<sup>4</sup> is hydrogen, halo, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkoxy are independently selected from halogeno, cyano, nitro, C<sub>1-3</sub>all ylsulphanyl, N(OH)R<sup>13</sup> (wherein R<sup>13</sup> is hydrogen, or C<sub>1-2</sub>alkyl), or R<sup>14</sup>X<sup>1</sup> (wherein X<sup>4</sup> represents a direct bond, O<sub>1</sub>, CH<sub>2</sub>, OC(O), C(O), S<sub>1</sub>, SO<sub>1</sub>, SO<sub>2</sub>, NR<sup>13</sup>, NR<sup>18</sup>SO<sub>3</sub> or NR<sup>19</sup> (wherein R<sup>46</sup>, R<sup>16</sup>, R<sup>47</sup>, R<sup>48</sup> and R<sup>46</sup> each independently represents hydrogen, C<sub>1-2</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl)), and R<sup>44</sup> is hydrogen, eptionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy

and n is 0, or an integer of fro n 1 to 6,

R<sup>55</sup> is halo, cyano, nitro, triflucromethyl, C<sub>1-3</sub>alkyl, -NR<sup>12</sup>R<sup>15</sup> [(]]wherein R<sup>12</sup> and R<sup>13</sup>, which may be the same or different, each represents hydrogen or C1.3alkyl[[]], or a group -X1R14 [[(]]wherein X¹ represents a direct bond, -\;-, -CH<sub>2</sub>-, -OC(O)-, -C(O)-, -S-, -SO-, -SO<sub>2</sub>-, -NR¹5C(O)-, -C(O)NR<sup>16</sup>-, -SO<sub>2</sub>NR<sup>17</sup>-, -NR<sup>18</sup>SO<sub>2</sub>- or -NR<sup>18</sup>- [[(]]wherein R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl[])]], and R<sup>14</sup> is hydrogen or C1-salkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, oxiramil, fluoro, chloro, bromo and amino including C1-salkyl and trifluoromethyl; or -RaR38 and wherein R38 represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group linked via carbon or nitrogen with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents selected from hydroxy, nitro, halogeno, amino, C, alkyl, C, alkoxy, C1-4hydroxyalkyl, C1-aminoalkyl, C1-alkylamino, C1-4hydroxyalkoxy, oxo, cyanoC1-alkyl, cyclopropyl, C1-alkvisulphonylC1-alkvi, C1-alkoxycarbonyl, di(C1-alkyl)amino, C1.4alkylaminoC1.4alkyl, C1.4alkanoyl, di(C1.4alkyl)aminoC1.4alkyl, C1.4alkylaminoC1.4alkyx. di(C1-alkvi)aminoC1-alkoxy, carboxy, carboxamido, trifluoromethyl, cyano, -C(O)NR39R40 -NR<sup>41</sup>C(O)R<sup>42</sup> wherein R<sup>39</sup>, R<sup>41</sup>, R<sup>41</sup> and R<sup>42</sup>, which may be the same or different, each represents hydrogen, C1-alkyl, hydroxyC1-alkyl or C1-alkoxyC2-alkyl and a group -(-O-)<sub>f</sub>(C<sub>1-4</sub>alkyl)<sub>e</sub>ringD wherein f is 0 or 1, g is 0 or 1 and ring D is a cyclic group selected from Czecycloalkyl, aryl or 5-6-merr bered saturated or unsaturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which cyclic group may bear one or more substituents selected from halp and C1-alkyl; and wherein Rº is a C1-alkylene group optionally

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Application No. 10/088,354 Amendment Dated 08/12/2005 Reply to Office Action of 03/14/2005

substituted by one or more substituents selected from hydroxy, halogeno and amino hydrogen, optionally substituted hydrocurbyl, optionally substituted hoterocyclyl-or optionally substituted alkexy;

and R<sup>57</sup> is C<sub>1-8</sub>alkoxy eptionally substituted with a group X<sup>1</sup>R<sup>38</sup> [[(]]wherein X<sup>1</sup> represents a direct bend, O, CH<sub>2+</sub>OC(O), C(O), S, SO, SO<sub>2</sub>, NR<sup>45</sup>C(O), C(O)NR<sup>48</sup>, SO<sub>2</sub>NR<sup>47</sup>, NR<sup>48</sup>SO<sub>2</sub>, or NR<sup>49</sup> (wherein R<sup>48</sup>, R<sup>45</sup>, R<sup>45</sup>, R<sup>48</sup> and R<sup>40</sup> each independently represents hydrogen, C<sub>1-2</sub>alkyl or C<sub>1-2</sub>alkylwyC<sub>2-2</sub>alkyl)), and R<sup>38</sup> are as defined above is a pyridene group, an anyl group or an aromatic heterocyclic group (linked via carbon or nitrogen) with 1–3 heteroatoms selected from O<sub>1</sub> N and S, which pyridene, anyl or aromatic heterocyclic group may be substituted by one or more functional groups or by a hydrocarbyl group optionally substituted by one or more functional groups or hydrocarbyl groups, or R<sup>67</sup> is 3-morpholinopropoxy; provided that R<sup>62</sup> is other than unsubstituted alkoxy; or a compound of formula (IIII3)

or a salt, ester, amide or prodiug thereof,

where X, R<sup>4</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>7</sup> and as defined above, and R<sup>68</sup> are R<sup>67</sup> are as defined above provided that R<sup>67</sup> is other than unsubstituted alkoxy; and R<sup>61</sup> is benzyl or cyanobenzyl or R<sup>61</sup> is optionally substituted phenyl, where the optional substituents include C<sub>1-3</sub> alkyl groups as well as nitro and halo or R<sup>61</sup> is ethynyl optionally substituted with trimethylsilyl groups, carboxy, or an C<sub>1-6</sub> alkyl ester thereof;

er empound of formula (IVB)

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or a salt, ester, amide or prodrug thereof,

where X, R<sup>4</sup>, R<sup>4</sup> and R<sup>7</sup> and n are as defined above, R<sup>62</sup> is a group of formula NR<sup>40</sup>R<sup>40</sup> where R<sup>40</sup> and R<sup>40</sup> are independently selected from hydrogen, optionally substituted hydrocarbyl or optionally substituted heterocyclyl, or R<sup>40</sup> and R<sup>40</sup> together with the nitrogen atom to which they are attached form an optionally substituted heterocyclic ring which may optionally contain further heterostoms, or an azo group of formula—N=N-R<sup>44</sup> where R<sup>44</sup> is an optionally substituted hydrocarbyl group or optionally substituted heterocyclyl group, or R<sup>62</sup> is a group—N=NR<sup>44</sup> where R<sup>44</sup> is as defined above, and Ft<sup>66</sup> are R<sup>65</sup> are as defined above provided that R<sup>67</sup> is other than unsubstituted alkexy;

er a-compound-of-formula (IVC)

or a salt, oster, amide or produg thereof,
where R<sup>4</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>4</sup> and X are as defined in claim 1.

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	☐ Helped examiner better unders	stand the state of the art in their technology.
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> Relev	vant prior art <b>not found:</b>	
	Results verified the lack of relevant pr	ior art (helped determine patentability).
	Results were not useful in determining	g patentability or understanding the invention.
Commen	nts:	

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```
26 27 29 31 32 35 36 40
    11 12 13 14 15 16
                            17 24
ring nodes :
    1 2 3 4 5 6 7 8 9
ring/chain nodes :
    28 30
chain bonds :
    7 - 11 \quad 11 - 24 \quad 14 - 15 \quad 16 - 17 \quad 24 - 40 \quad 26 - 28 \quad 27 - 30 \quad 28 - 29 \quad 30 - 31 \quad 30 - 32
ring bonds :
    1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
    5-7 6-10 7-8 7-11 8-9 9-10 11-24 14-15 16-17 24-40 26-28 27-30 28-29 30-31
    30-32
normalized bonds :
    1-2 1-6 2-3 3-4 4-5 5-6
G1: [*1], [*2], [*3], [*4]
G2: [*5], [*6], [*7], [*8]
Connectivity:
    8:2 E exact RC ring/chain 10:2 E exact RC ring/chain 29:1 E exact RC ring/chain
```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 24:Atom 26:CLASS 27:CLASS

28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 35:CLASS 36:CLASS 40:CLASS

chain nodes :

Match level :

Generic attributes :

24:

Saturation : Unsaturated Number of Carbon Atoms : less than 7 Type of Ring System : Monocyclic

Element Count :

Node 24: Limited

C,C6

C:\Program Files\Stnexp\Queries\10 088854\tru-g.str 490 12 48 0 11 001 1:0 1 12<sup>0</sup> 2 se<sup>2</sup> N @ 3 1:<sup>@</sup> 3 85@ 19 \_SE.@ 20

chain nodes :

28 29 30 31 33 34 35 36 37 27 22 23 24 25 26 11 12 13 18 20 21 83 84 90 92 93 95 96 98 78 39 40 48 49 61 62 63 64 73 74 75 76 77

ring nodes :

1 2 3 4 5 6 7 8 9 10 42 43 44 45 46 47

chain bonds :

7-90 18-90 18-98 20-92 21-93 22-61 23-63 24-25 26-27 27-28 29-30 30-31 33-34 35-36 36-37 38-39 39-40 61-62 62-95 63-64 64-96 73-75 74-76 75-77 76-78

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 42-43 42-47 43-44 44-45 45-46 46-47

exact/norm bonds :

5-7 6-10 7-8 7-90 8-9 9-10 18-90 18-98 20-92 21-93 24-25 26-27 27-28 29-30 30-31 33-34 35-36 36-37 38-39 39-40 62-95 64-96

exact bonds :

22-61 23-63 61-62 63-64 73-75 74-76 75-77 76-78

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 42-43 42-47 43-44 44-45 45-46 46-47

G1: [\*1], [\*2], [\*3]

G2: [\*4], [\*5], [\*6], [\*7], [\*8], [\*9]; [\*10], [\*11], [\*12]

G3: [\*13], [\*14], [\*15], [\*16], [\*17], [\*18], [\*19], [\*20]

Connectivity :

```
8:2 E exact RC ring/chain 10:2 E exact RC ring/chain 24:2 E exact RC ring/chain
   25:1 E exact RC ring/chain 26:2 E exact RC ring/chain 27:2 E exact RC ring/chain
   28:1 E exact RC ring/chain 29:2 E exact RC ring/chain 30:2 E exact RC ring/chain
   31:1 E exact RC ring/chain 33:2 E exact RC ring/chain 34:1 E exact RC ring/chain
   35:2 E exact RC ring/chain 36:2 E exact RC ring/chain 37:1 E exact RC ring/chain
   38:2 E exact RC ring/chain 39:2 E exact RC ring/chain 40:1 E exact RC ring/chain
Match level :
   1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
   12:CLASS 13:CLASS 18:Atom 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS
   26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 33:CLASS 34:CLASS 35:CLASS
    36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 42:Atom 43:Atom 44:Atom 45:Atom
    46:Atom 47:Atom 48:Atom 49:Atom 61:CLASS 62:CLASS 63:CLASS 64:CLASS 73:CLASS
    74:CLASS 75:CLASS 76:CLASS 77:CLASS 78:CLASS 83:CLASS 84:CLASS 90:CLASS 92:CLASS
   93:CLASS 95:CLASS 96:CLASS 98:CLASS
Generic attributes :
   18:
   Saturation
                         : Unsaturated
   Number of Carbon Atoms : less than 7
   Type of Ring System
                       : Monocyclic
   48:
   Saturation
                        : Unsaturated
   Number of Carbon Atoms : less than 7
   Number of Hetero Atoms : less than 2
   Type of Ring System
                       : Monocyclic
   49:
   Saturation
                        : Unsaturated
   Number of Carbon Atoms : less than 7
   Number of Hetero Atoms : less than 2
   Type of Ring System : Monocyclic
Element Count :
   Node 18: Limited
       C,C6
```

Node 48: Limited C,C5 N,N1

Node 49: Limited C,C4 O,O1 C:\Program Files\Stnexp\Queries\10 088854\tru-h.str\_

chain nodes :

34 37 38 39 40 42 46 47 48 33 36 41 12 13 15 20 22 23 24 31 70 51 52 53 54 55 56 57 59 60 62 63 64 65 66 67 69 83

ring nodes :

1 2 3 4 9 10 25 26 27

chain bonds :

 $1-20 \quad 2-23 \quad 7-22 \quad 13-15 \quad 23-24 \quad 24-83 \quad 31-33 \quad 36-59 \quad 37-60 \quad 38-39 \quad 38-40 \quad 38-62 \quad 41-42$ 41-63 46-64 47-48 48-49 48-65 50-51 50-52 52-66 53-54 54-67 55-56 56-69 57-70 ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 25-26 25-30 26-27 27-28 28-29 29-30

exact/norm bonds :

1-20 2-23 5-7 6-10 7-8 7-22 8-9 9-10 13-15 23-24 24-83 31-33 36-59 37-60 38-39 38-40 38-62 41-42 41-63 46-64 47-48 48-49 48-65 50-51 50-52 52-66 53-54 54-67 55-56 56-69 57-70

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 25-26 25-30 26-27 27-28 28-29 29-30

G1:H,X,[\*1],[\*2]

G2:0,S,N

G3: [\*3], [\*4], [\*5]

G4: [\*3], [\*4], [\*5], [\*6], [\*7], [\*8], [\*9], [\*10], [\*11], [\*12], [\*13], [\*14], [\*15]

Connectivity:

4:2 E exact RC ring/chain 8:2 E exact RC ring/chain 10:2 E exact RC ring/chain 12:2 X maximum RC ring/chain 13:2 X maximum RC ring/chain 33:1 E exact RC ring/chain Match level : 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 12:CLASS 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom 13:CLASS 15:CLASS 20:CLASS 22:CLASS 28:Atom 29:Atom 30:Atom 31:Atom 33:CLASS 34:Atom 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS 52:CLASS 53:CLASS 54:CLASS 55:CLASS 56:CLASS 57:CLASS 59:CLASS 60:CLASS 62:CLASS 63:CLASS 64:CLASS 65:CLASS 66:CLASS 67:CLASS 69:CLASS 70:CLASS 83:CLASS Generic attributes : 31: : Unsaturated Saturation Number of Carbon Atoms : less than 7

Number of Hetero Atoms : less than 2 Type of Ring System : Monocyclic

34:

Saturation : Unsaturated Number of Carbon Atoms : less than 7 Type of Ring System : Monocyclic

#### Element Count :

Node 12: Limited C, C1-4

Node 13: Limited C, C1-4

Node 24: Limited C, C1-8

Node 31: Limited C, C5 N,N1

Node 34: Limited

C, C2-5 0,00-3

N, N0-3

S, S0-3

Structure Search in Registry
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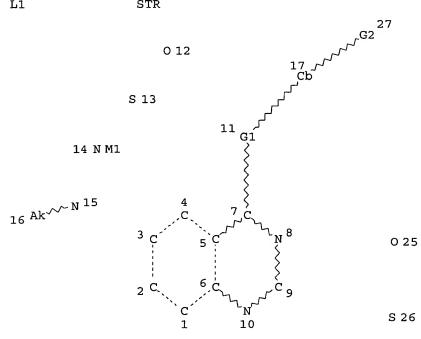
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Effective October 17, 2005, revised CAS Information Use Policies apply.

They are available for your review at:

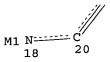
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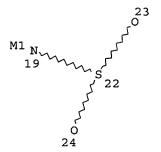
=> d stat que L15 L1 STR





Page 1-A





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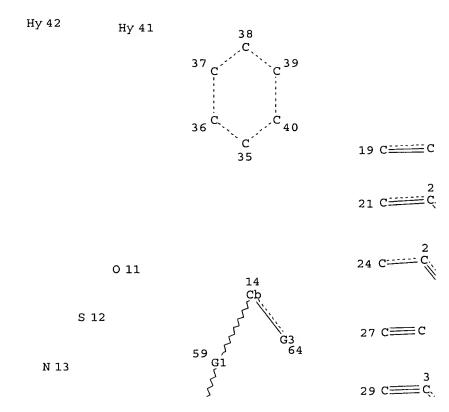
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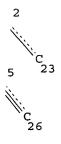
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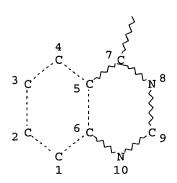
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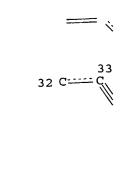


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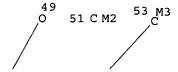
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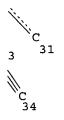


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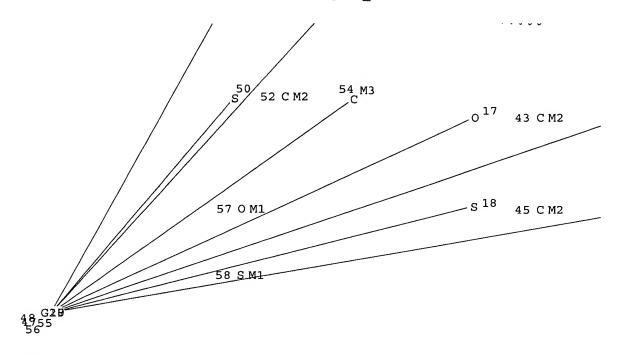


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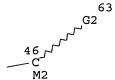


Page 2-B



Page 3-A





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Structure attributes must be viewed using STN Express query preparation.
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FILE 'USPAT2' ENTERED AT 14:48:22 ON 18 OCT 2005
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FILE 'TOXCENTER' ENTERED AT 14:48:22 ON 18 OCT 2005
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PROCESSING COMPLETED FOR L15
PROCESSING COMPLETED FOR L23

L24 15 DUP REM L15 L23 (7 DUPLICATES REMOVED)

ANSWERS '1-8' FROM FILE CAPLUS ANSWERS '9-15' FROM FILE USPATFULL

## => d ibib abs hitstr L24 1-15

L24 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2002:888722 CAPLUS

DOCUMENT NUMBER: 137:384857

TITLE: Preparation of 4-anilinoquinazolines as antitumor

agents

INVENTOR(S): Hennequin, Laurent François Andre; Ple, Patrick PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO			KIND DATE				1	APPL	ICAT:		DATE				
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T	J, TM														
RW: GH	H, GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑT,	BE,	CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRIORITY APPLN. INFO.: EP 2001-401221 A 20010514 OTHER SOURCE(S): MARPAT 137:384857

R3 HIN OME

AB The title compds. [I; R1 = H, OH, alkoxy and R2 = hydroxyalkoxy, alkoxyalkoxy, aminoalkoxy, etc.; or R2 = H, OH, alkoxy and R1 = hydroxyalkoxy, alkoxyalkoxy, aminoalkoxy, etc.; R3 = Cl, Br, I], useful as an anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of I.2HCl [R1 = OMe; R2 = 3-(4-methylpiperazin-1-yl)propoxy; R3 = Cl], starting from 2-amino-4-benzyloxy-5-methoxybenzamide, was given. The biol. activity of compds. I was tested in 4 tests. Thus, the compds. I showed IC50 of 0.001-10 μM in in vitro c-Src tyrosine kinase assay.

IT 476156-86-2P, 7-Benzyloxy-4-(2-chloro-5-methoxyanilino)-6-methoxyquinazoline

Ι

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 4-anilinoquinazolines as antitumor agents)

RN 476156-86-2 CAPLUS

CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-6-methoxy-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:888720 CAPLUS

DOCUMENT NUMBER: 137:384855

TITLE: Preparation of 4-anilinoquinazolines as antitumor

agents

INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE:

Hennequin, Laurent Francois Andre; Ple, Patrick Astrazeneca AB, Swed.; Astrazeneca UK Limited PCT Int. Appl., 96 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

GI

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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	TJ, TM														
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PRIORITY APPI	JN. INFO	).:						EP 2	001-	4012	23	i	A 20	0010	514
OTHER SOURCE		MARPAT 137:38485													
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 $OMe$ 
 $R^2$ 
 $N$ 

The title compds. [I; R1 = H, alkoxy and R2 = X1Q1 (wherein X1 = O, S, SO, etc.; Q1 = heteroaryl, heteroarylalkyl, heterocyclyl, etc.), X2R5 (wherein X2 = O, NH, Nalkyl; R5 = hydroxyalkyl, alkoxyalkyl, aminoalkyl, etc.); or R2 = H, alkoxy and R1 = X1Q1, X2R5; R3 = Cl, Br, I], useful as anti-invasive agents in the containment and/or treatment of solid tumor disease, were prepared and formulated. E.g., a multi-step synthesis of I [R1 = OMe; R2 = N-methylpiperidin-4-ylmethoxy; R3 = Cl], starting from Et piperidine-4-carboxylate, was given. Biol. activity of compds. I was tested in 4 tests. Thus, the compds. I showed IC50 of 0.001-10 μM in in vitro c-Src tyrosine kinase assay.

IT 476160-08-4P, 4-(2-Chloro-5-methoxyanilino)-6-methoxy-7-[2-(4-pyridyloxy)ethoxy]quinazoline 476160-09-5P 476160-10-8P 476160-11-9P 476160-12-0P 476160-13-1P 476160-14-2P 476160-15-3P 476160-27-7P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

Ι

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-anilinoquinazolines as antitumor agents)

RN 476160-08-4 CAPLUS

CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-6-methoxy-7-[2-(4pyridinyloxy)ethoxy]- (9CI) (CA INDEX NAME)

RN 476160-09-5 CAPLUS

CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-6-methoxy-7-[3-(4-pyridinyloxy)propoxy]- (9CI) (CA INDEX NAME)

RN 476160-10-8 CAPLUS

CN 4-Quinazolinamine, N-(2-bromo-5-methoxyphenyl)-6-methoxy-7-[2-(4-pyridinyloxy)ethoxy]- (9CI) (CA INDEX NAME)

RN 476160-11-9 CAPLUS

CN 4-Quinazolinamine, N-(2-bromo-5-methoxyphenyl)-6-methoxy-7-[3-(4-pyridinyloxy)propoxy]- (9CI) (CA INDEX NAME)

RN 476160-12-0 CAPLUS

CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-6-methoxy-7-[3-(2-pyridinyloxy)propoxy]- (9CI) (CA INDEX NAME)

RN 476160-13-1 CAPLUS

CN 3-Pyridinecarbonitrile, 4-[[[4-[(2-chloro-5-methoxyphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

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RN 476160-14-2 CAPLUS

CN 3-Pyridinecarbonitrile, 4-[[[4-[(2-bromo-5-methoxyphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

RN 476160-15-3 CAPLUS

CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-6-methoxy-7-[2-[5-methyl-2-(4-morpholinylmethyl)-1H-imidazol-1-yl]ethoxy]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} O \\ N \\ CH_2 \\ N \\ N \\ CH_2 \\ CH_2 \\ CH_2 \\ O \\ MeO \\ N \\ N \\ NH \\ C1 \\ MeO \\ C1 \\ \end{array}$$

RN 476160-27-7 CAPLUS

CN 1(2H)-Pyridineethanol, α-[[[4-[(2-chloro-5-methoxyphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-3,6-dihydro- (9CI) (CA INDEX NAME)

IT 476156-86-2P, 7-Benzyloxy-4-(2-chloro-5-methoxyanilino)-6-

methoxyquinazoline 476160-50-6P, 4-(2-Bromo-5-methoxyanilino)-7-

benzyloxy-6-methoxyquinazoline

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of 4-anilinoquinazolines as antitumor agents)

RN 476156-86-2 CAPLUS

CN 4-Quinazolinamine, N-(2-chloro-5-methoxyphenyl)-6-methoxy-7-

(phenylmethoxy) - (9CI) (CA INDEX NAME)

RN 476160-50-6 CAPLUS

CN 4-Quinazolinamine, N-(2-bromo-5-methoxyphenyl)-6-methoxy-7-(phenylmethoxy)(9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2001:228864 CAPLUS

DOCUMENT NUMBER: 134:252355

TITLE: Preparation of quinazolines as aurora 2 kinase

inhibitors

INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas John

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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TR 200200749 T2 20020621 TR 2002-200200749		
EP 1218356 A1 20020703 EP 2000-962677		20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU,	NL, S	SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL		
JP 2003509497 T2 20030311 JP 2001-524973		20000918
EE 200200149 A 20030415 EE 2002-149		20000918
AU 763242 B2 20030717 AU 2000-74325		20000918
ZA 2002001833 A 20030605 ZA 2002-1833		20020305
BG 106491 A 20021229 BG 2002-106491		20020307
NO 2002001401 A 20020521 NO 2002-1401		
PRIORITY APPLN. INFO.: GB 1999-22152	Α	19990921
GB 1999-22156		19990921
GB 1999-22159		
WO 2000-GB3556	W	20000918

OTHER SOURCE(S):

MARPAT 134:252355

GI

$$R^2$$
 $R^3$ 
 $R^4$ 
 $R^4$ 

Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR8; R8 = H or alkyl; AB Ra = (un) substituted 3-quinolinyl or Ph; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R12, or R14X1; R12 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un) substituted NHCO, CONH, SO2NH, NHSO2, or NH; R14 = H or (un) substituted hydrocarbyl, heterocyclyl, or alkoxy; or a salt, ester, or amide thereof] were prepared as aurora 2 kinase

II

inhibitors for the treatment of proliferative diseases, such as cancer. For example, 4-phenoxyaniline  $\bullet$ HCl and 4-chloro-6-methoxy-7-(3-morpholinopropoxy) quinazoline were refluxed in i-PrOH to yield II (86%). The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration of 0.069  $\mu$ M. In addition, II gave 50% inhibition of MCF-7 cell proliferation at 2.89  $\mu$ M and reduced BrdU incorporation into cellular DNA by 50% at 3.68  $\mu$ M.

IT 330999-51-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-substituted quinazoline aurora 2 kinase inhibitors by coupling quinolinyl or Ph alcs., thiols, or amines with 4-haloguinazolines)

RN 330999-51-4 CAPLUS

CN 4-Quinazolinamine, 6-methoxy-N-(4-phenoxyphenyl)-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5

ACCESSION NUMBER:

2000:733043 CAPLUS

DOCUMENT NUMBER:

133:281796

TITLE:

Method for preparation of anticancer

4-(3-ethynylphenylamino)quinazoline derivatives and

intermediates thereof

INVENTOR(S):

Lehner, Richard Shelton; Norris, Timothy; Santafianos,

Dinos Paul

PATENT ASSIGNEE(S):

Pfizer Products Inc., USA

SOURCE:

Jpn. Kokai Tokkyo Koho, 15 pp.

CODEN: JKXXAF

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000290262	A2	20001017	JP 2000-91300	20000329
JP 3420549	B2	20030623		
EP 1044969	A2	20001018	EP 2000-302256	20000320
EP 1044969	A3	20001129		

	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	٤, :	ΙT,	LI,	LU,	NL,	SE	, MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO											
BR	2000	0014	86		Α		2001	0502	:	BR	20	00-	1486				20000	327
EG	2250	6			Α	- 2	2003	0331		EG	20	00-	364				20000	327
TW	5539	39			В	- 2	2003	0921	•	TW	20	00-	8910	5605			20000	327
BG	1042	78			Α	2	2001	0831	:	BG	20	00-	1042	78			20000	328
AU	7814	02			B2	2	2005	0519		ΑU	20	00-	2262	0			20000	328
CA	2302	965			AA	2	2000	0930		CA	20	00-	2302	965			20000	329
CA	2302	965			C	2	2004	0217										
CA	2427	221			AA	2	2000	0930	(	CA	20	00-	2427	221			20000	329
ZA	2000	0015	86		Α	- 2	2001	1001		ZA	20	00-	1586				20000	329
JP	2003	1762	74		A2	2	2003	0624	,	JP	20	02~	3607	42			20000	329
NO	2000	0016	48		Α	2	2000	1002	]	ОИ	20	00-	1648				20000	330
TR	2000	0083	7		A2	2	2000	1121	•	TR	20	00-	2000	0083	7		20000	330
EE	2000	0025	5		Α	2	2000	1215		EE	20	00-3	255				20000	330
NZ	5036	83			Α	2	2001	0928	]	NZ	20	00-	5036	83			20000	330
ບຣ	6476	040			В1	2	2002	1105	1	US	20	00-	5386	35			20000	330
NZ	5128	18			Α	2	2003	0131	]	NZ	20	00-	5128	18			20000	330
CN	1276	370			Α	2	2000	1213	(	CN	20	00-1	1045	95			20000	331
HR	2000	0001	82		A1	2	2001	0430	]	HR	20	00-1	182				20000	331
PRIORITY	APP:	LN.	INFO	. :					1	US	19	99-:	1270	72P		Ρ	19990	331
									(	CA	20	00-3	2302	965		А3	20000	329
										JP	20	00-	9130	0		А3	20000	329
									]	NZ	20	00-	5036	83		A1	20000	330

OTHER SOURCE(S):

CASREACT 133:281796; MARPAT 133:281796

$$R^{15}$$
 $N$ 
 $C \equiv C - G$ 

The title compds. [I; G = H; R1, R2 = C1-10 alkyl or alkoxy each optionally substituted by ≤2 groups selected from HO or C1-6 alkoxy; R15 = H, C1-10 alkyl, C6-10 aryl-(CH2)q; q = 0-4], pharmacol. acceptable salts or solvates thereof, which are useful as anticancer agents (no data), are prepared by treatment of I [G = C(OH)R3R4 protecting group; R3, R4 = C1-6 alkyl] with alkali or alkaline earth metal hydroxide in a solvent containing hydroxy-C1-10 group or treatment of I (G = SiR3R4R5 protecting group; R3, R4, R5 = C1-6 alkyl) with tetra(C1-6 alkyl)ammonium fluoride in an aprotic solvent. Thus, 4-chloro-6,7-bis(2-methoxyethoxy)quinazoline was treated with 3-[(trimethylsilyl)ethynyl]anil ine in 2-propanol and refluxed for 2.5 h to give 88% I.HCl (G = trimethylsilyl, R1 = R2 = 2-methoxyethoxy, R15 = H) which was stirred with Bu4NF in THF at room temperature for 1 h to give 72% I.HCl (G = R15 = H, R1 = R2

Ι

= 2-methoxyethoxy).

## IT 299912-65-5P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method for preparation of anticancer (ethynylphenylamino)quinazoline

derivs. and intermediates thereof)

299912-65-5 CAPLUS RN

4-Quinazolinamine, 6-(2-methoxyethoxy)-N-(4-methoxyphenyl)-7-CN (phenylmethoxy) - (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Ph-CH}_2\text{-O} \\ \text{MeO-CH}_2\text{-CH}_2\text{-O} \\ \end{array}$$

L24 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1997:640511 CAPLUS

DOCUMENT NUMBER: 127:278209

Preparation of 4-anilinoquinazolines for use in the TITLE:

> treatment of disease states associated with antiangiogenesis and/or increased vascular

permeability

INVENTOR(S): Thomas, Andrew Peter; Hennequin, Laurent Francois

Andre; Johnstone, Craig Zeneca Ltd., UK; Zeneca Pharma S.A.; Thomas, Andrew PATENT ASSIGNEE(S):

Peter; Hennequin, Laurent Francois Andre; Johnstone,

Craig

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.			KIN	D 1	DATE			APPL	ICAT		DATE				
WO 9732	856	<del>-</del>		A1	_	 1997	0912		 WO 1	 997-(	 GB55	0		1:	 9970:	228
W:	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
	DK,	EE,	ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,
	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,
	RO,	RU,	SD,	SE,	SG,	SI,	SK,	ΤJ,	TM,	TR,	TT,	UA,	UG,	US,	UZ,	VN,
	YU,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	$\mathbf{TM}$						
RW:	GH,	ΚE,	LS,	MW,	SD,	SZ,	UG,	ΑT,	ΒE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,
	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,
	ML,	MR,	NE,	SN,	TD,	TG										
ZA 9701	.747			Α		1998	0827		ZA 1	997-	1747			1:	9970:	227
CA 2244	897			AA		1997	0912		CA 1	997-	2244	897		1:	9970:	228
AU 9718	664			A1		1997	0922		AU 1	997-	1866	4		1:	9970:	228
AU 7193	27			B2	:	2000	0504									
EP 8851	.98		-	A1		1998	1223		EP 1	997-	9068	14		1	9970	228
EP 8851	.98			B1	:	2001	1219									
R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,

IE, FI					
CN 1212684	Α	19990331	CN 1997-192807		19970228
CN 1116286	В	20030730			
NZ 331191	Α	20000327	NZ 1997-331191		19970228
JP 2000517291	T2	20001226	JP 1997-531552		19970228
AT 211134	E	20020115	AT 1997-906814		19970228
PT 885198	T	20020628	PT 1997-906814		19970228
ES 2169355	<b>T</b> 3	20020701	ES 1997-906814		19970228
IL 125954	A1	20030624	IL 1997-125954		19970228
TW 542826	В	20030721	TW 1997-861025	93	19970304
NO 9804085	Α	19980904	NO 1998-4085		19980904
NO 311427	B1	20011126			
US 6291455	B1	20010918	US 1998-142339		19980908
PRIORITY APPLN. INFO.:			EP 1996-400468	Α	19960305
			EP 1996-401499	Α	19960708
			WO 1997-GB550	W	19970228

OTHER SOURCE(S): MARPAT 127:278209

GΙ

$$\begin{bmatrix} R^{3} \end{bmatrix}_{2}$$

$$\begin{bmatrix} R^{2} \end{bmatrix}_{N}$$

$$\begin{bmatrix} R^{3} \end{bmatrix}_{2}$$

The title compds. [I; R1 = H, MeO; R2 = MeO, EtO, 2-MeO(CH2)2O, etc.; R3 = halo, OH, CN, etc.] and their salts, inhibiting the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis, were prepared and formulated. Thus, reaction of 4-chloro-7-(2-methoxyethoxy)quinazoline.HCl with 4-chloro-2-fluoroaniline in iPrOH afforded 84% I [R1 = H; R2 = 2-MeO(CH2)2O; R3 = 4-Cl, 2-F]. Compds. I are effective at 1-50 mg/kg. IT 196603-79-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 4-anilinoquinazolines for use in the treatment of disease states associated with antiangiogenesis and/or increased vascular permeability)

RN 196603-79-9 CAPLUS

CN Phenol, 5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

L24 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 1997:675952 CAPLUS

DOCUMENT NUMBER: 127:262698

TITLE: Preparation of quinazolines as VEGF inhibitors INVENTOR(S): Thomas, Andrew Peter; Johnstone, Craig; Hennequin,

Laurent Francois Andre

PATENT ASSIGNEE(S): Zeneca Ltd., UK; Zeneca Pharma S.A.; Thomas, Andrew

Peter; Johnstone, Craig; Hennequin, Laurent Francois

Andre

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	ENT	NO.			KINI	<b>D</b> 1	DATE APPLICATION NO.								D	ATE	
WO	9730	035			A1	_	1997	0821	,	WO :	1997-	GB36	5		1:	9970	210
											, CA,					DE,	DK,
											, KE,						
											, MX,						
											, UA,						
		AZ,	BY,	KG,	ΚZ,	MD,	RU,	TJ,	TM								
	RW:	KΕ,	LS,	MW,	SD,	SZ,	UG,	AT,	BE,	CH	, DE,	DK,	ES,	FI,	FR,	GB,	GR,
											, CF,						
					TD,												
	2242										1997-						
ΑU	9717									AU :	1997-	1729	0		1:	9970	210
ΑU	7194				B2												
ΕP	8805				A1					EP :	1997-	9045	12		1:	9970	210
ΕP	8805				B1												
	R:							FR,	GB,	GR	, IT,	LI,	LU,	ΝL,	SE,	MC,	PT,
				•	LV,	•									_		
	1211				Α			0317		CN :	1997-	1922	21		1:	9970	210
	1125				В		2003	1029							_		
	9707				A						1997-					9970	
	3308				Α		2000				1997-					9970	
	2000				T2		2000				1997-					9970	
	1256						2002				1997-					9970	
	2196						2003				1998-					9970	
	2913						2003	-			1998-					9970	
ΑT	2375	96			E		2003	0515		AT'	1997-	9045	12		1:	9970	210

PT 880508	T	20030731	PT	1997-904512		19970210
ES 2194181	Т3	20031116	ES	1997-904512		19970210
ZA 9701180	Α	19970813	ZA	1997-1180		19970212
TW 581765	В	20040401	TW	1997-86101670		19970212
NO 9803687	Α	19980813	NO	1998-3687		19980812
NO 311359	B1	20011119				
US 6184225	B1	20010206	US	1998-125271		19980813
HK 1016607	A1	20030926	HK	1999-101774		19990421
PRIORITY APPLN. INFO.:			EP	1996-400293	Α	19960213
			EP	1996-401756	Α	19960808
			EP	1996-402764	A	19961217
			WO	1997-GB365	W	19970210

OTHER SOURCE(S):

MARPAT 127:262698

GΙ

$$\begin{bmatrix} R^{2} & Z & & \\ R^{3} \end{bmatrix}_{m}$$

$$R^{4}-X^{1}$$

The title compds. [I; Z = O, NH, S; m = 1-5; R1 = H, OH, halo, etc.; R2 = H, OH, halo, etc.; R3 = OH, halo, C1-3 alkyl, etc.; X1 = O, CH2, S, etc.; R4 = H, C1-5 alkyl, C1-5 hydroxyalkyl, etc.] and their salts which inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis, were prepared and formulated. Thus, reaction of 4-chloro-6,7-dimethoxyquinazoline with 4-bromo-2-fluoro-5-hydroxyaniline in the presence of isopropanolic hydrogen chloride in 2-butanol afforded 87% quinazoline II.HC1. Compds. I are effective at 1-50 mg/kg.

#### IT 192999-96-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of quinazolines as VEGF inhibitors)

RN 192999-96-5 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-

quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

L24 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1999:784580 CAPLUS

DOCUMENT NUMBER: TITLE:

132:151769
Design and Structure-Activity Relationship of a New

Class of Potent VEGF Receptor Tyrosine Kinase

Inhibitors

AUTHOR(S):

Hennequin, Laurent F.; Thomas, Andrew P.; Johnstone, Craig; Stokes, Elaine S. E.; Ple, Patrick A.; Lohmann, Jean-Jacques M.; Ogilvie, Donald J.; Dukes, Mike;

Wedge, Steve R.; Curwen, Jon O.; Kendrew, Jane;

CORPORATE SOURCE:

AstraZeneca Zeneca Pharma Centre de Recherches Z.I. La

Pompelle, Reims, 51689, Fr.

SOURCE:

Journal of Medicinal Chemistry (1999), 42(26),

5369-5389

CODEN: JMCMAR; ISSN: 0022-2623

Lambert-van der Brempt, Christine

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

GI

AB A series of substituted 4-anilinoquinazolines and related compds. were synthesized as potential inhibitors of vascular endothelial growth factor

(VEGF) receptor (Flt and KDR) tyrosine kinase activity. Enzyme screening indicated that a narrow structure-activity relationship (SAR) existed for the bicyclic ring system, with quinazolines, quinolines, and cinnolines having activity and with quinazolines and quinolines generally being preferred. Substitution of the aniline was investigated and clearly indicated that small lipophilic substituents such as halogens or Me were preferred at the C-4' position. Small substituents such as hydrogen and fluorine are preferred at the C-2' position. Introduction of a hydroxyl group at the meta position of the aniline produced the most potent inhibitors of Flt and KDR tyrosine kinases activity with IC50 values in the nanomolar range. Investigation of the quinazoline C-6 and C-7 positions indicates that a large range of substituents are tolerated at C-7, whereas variation at the C-6 is more restricted. At C-7, neutral, basic, and heteroarom. side chains led to very potent compds., as illustrated by the methoxyethoxy derivative I [R1 = 4-C1, R2 = OCH2CH2OMe] (IC50 < 2 nM). These inhibitors proved to be very selective inhibitors of Flt and KDR tyrosine kinase activity when compared to that associated with the FGF receptor (50- to 3800-fold). Observed enzyme profiles translated well with respect to potency and selectivity for inhibition of growth factor stimulated proliferation of human umbilical vein endothelial cells (HUVECs). Oral administration of selected compds. to mice produced total plasma levels 6 h after dosing of between 3 and 49  $\mu M$ . In vivo efficacy was demonstrated in a rat uterine edema assay where significant activity was achieved at 60 mg/kg with I [R1 = Me, R2 = OMe]. Inhibition of growth of human tumors in athymic mice has also been demonstrated: I [R1 = Br, R2 = 2 - (1, 2, 3 - triazol - 1 - yl) ethoxy] inhibited the growth of established Calu-6 lung carcinoma xenograft by 75% (P < 0.001, one tailed t-test) following daily oral administration of 100 mg/kg for 21 days. 192999-96-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and structure-activity relationship of arylaminoquinazoline VEGF receptor tyrosine kinase inhibitors)

RN 192999-96-5 CAPLUS

IT

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

HCl

REFERENCE COUNT:

79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1997:502972 CAPLUS

DOCUMENT NUMBER:

127:135808

TITLE:

Preparation and antiangiogenic and/or vascular permeability reducing effect of quinazoline

INVENTOR(S):

Lohmann, Jean-Jacques Marcel; Hennequin, Laurent

PATENT ASSIGNEE(S):

Francois Andre; Thomas, Andrew Peter Zeneca Limited, UK; Zeneca-Pharma S.A.; Lohmann, Jean-Jacques Marcel; Hennequin, Laurent Francois

Andre; Thomas, Andrew Peter

SOURCE:

PCT Int. Appl., 162 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

•		ENT				KIN	)	DATE			API	PLI	CAT	ION :	NO.		D.	ATE	
		9722						1997							 75		1	9961:	213
		W:	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BF	₹,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
			DK.	EE.	ES,	FI,	GB,	GE,	HU,	IL,	IS	3,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,
								LV,											
								sī,											
								MD,					•			-			
		RW:						UG,					DE,	DK,	ES,	FI,	FR,	GB,	GR,
								PT,											
			MR,	NE,	SN,	TD,	TG	•											
	CA	2237						1997							005		1	9961	213
	AU	9711	061			AA A1		1997			ΑU	19	97-	1106	1		1	9961	213
	ΑU	7123	70			B2		1999	1104										
	ΕP	8733	19			A1		1998	1028		ΕP	19	96-	9417	87		1	9961	213
	EP	8733	19			В1		2001	0725										
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	₹,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
			ΙE,	SI,	LT,	LV,	FI,	RO											
	CN	1205	694			Α		1999	0120		CN	19	96-	1991	10		1	9961	213
	CN	1133	625			В		2004	0107										
		9612				Α		1999	1228						3			9961	213
	JP	2000	5151	1.4		T2		2000	1114		JΡ	19	97-	5225	68		1	9961	213
	AT	2035 2162 8733 2824	24			E		2001	0815		AT	19	96-	9417	87		1	9961	213
	ES	2162	656			Т3		2002	0101		ES	19	96-	9417	87 87		1	9961	213
	PT	8733	19			T		2002	0130		PT	19	96-	9417	87		1	9961	
	SK	2824	43			В6		2002			SK	19	98-	828			1	9961	
		2911						2002										9961	
		2194						2002							00			9961	
		9610				Α		1997			ZA	19	96-	1059	7		1	9961	
		5962				Α		1999			US	19	96-	7688	87		1	9961	
		4112				В		2000			TW	19	96-	8511	5569			9961	
		9802				В А В1		1998			ИО	19	98-	2784			1	9980	617
		3113						2001											
		6071				Α		2000							64			9981	
		6258				B1		2001							70			0000	
		2002						2002			US	20	01-	8770	05		2	0010	611
		6362				B2		2002											
		3036				Т3		2002	0131		GR	20	01-	4018	23		2	0011 9951:	019
PRIO	RITY	APP	LN.	INFO	. :				•						46		A 1	9951	218
											ΕP	19	96-	4021	90		A 1	9961	015

EP 1996-941787 A 19961213 WO 1996-GB3075 W 19961213 US 1996-768887 A1 19961217 US 1998-203764 A1 19981202 US 2000-500470 A3 20000209

OTHER SOURCE(S):

MARPAT 127:135808

Quinazoline derivs. I [Y1 represents -O-, -S-, -CH2-, -SO-, -SO2-, NR5CO-, AB -CONR6-, -SO2NR7-, -NR8SO2- or -NR9- (wherein R5, R6, R7, R8 and R9 each independently represents hydrogen, alkyl or alkoxyalkyl); R1 represents hydrogen, hydroxy, halo, nitro, trifluoromethyl, cyano, alkyl, alkoxy, alkylthio, amino, alkylamino; R2 represents hydrogen, hydroxy, halo, alkyl, alkoxy, trifluoromethyl, cyano, amino, nitro; m is an integer from 1 to 5; R3 represents hydroxy, halo, alkyl, alkoxy, alkanoyloxy, trifluoromethyl, cyano, amino, nitro; R4 represents a group which is or which contains an optionally substituted pyridone, Ph or aromatic heterocyclic group] were prepared I inhibit the effects of VEGF (no data), a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis. E.g., heating a mixture of 2-amino-4-benzyloxy-5-methoxybenzamide and Gold's reagent, followed by NaOAc and HOAc, gave 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one. The product was treated with thionyl chloride, then 3-acetoxy-4methylaniline, and next hydrogenolyzed to give 4-(3-acetoxy-4methylanilino) - 7-hydroxy - 6-methoxyquinazoline hydrochloride. The last was reacted with 4-(bromomethyl) pyridine hydrobromide and treated with aqueous NaOH to give 4-(3-hydroxy-4-methylanilino)-6-methoxy-7-(4-

pyridylmethoxy) quinazoline hydrochloride. IT 192999-68-1P 192999-70-5P 192999-71-6P

192999-72-7P 192999-73-8P 192999-74-9P

Ι

192999-75-0P 192999-76-1P 192999-77-2P

192999-78-3P 192999-79-4P 192999-80-7P

192999-81-8P 192999-88-5P 192999-89-6P

192999-90-9P 192999-94-3P 192999-95-4P

192999-96-5P 192999-98-7P 192999-99-8P

193000-00-9P 193000-01-0P 193000-02-1P

193000-03-2P 193000-10-1P 193000-26-9P

193000-27-0P 193000-39-4P 193000-40-7P

193000-41-8P 193000-42-9P 193000-43-0P 193000-44-1P 193000-45-2P 193000-46-3P

193000-47-4P 193000-59-8P 193000-76-9P

193000-77-0P 193000-78-1P 193000-79-2P

193000-80-5P 193000-81-6P 193000-82-7P

```
193000-83-8P 193000-84-9P 193000-85-0P
     193000-86-1P 193000-87-2P 193000-88-3P
     193000-89-4P 193000-90-7P 193000-91-8P
     193000-92-9P 193000-93-0P 193000-94-1P
     193000-96-3P 193000-97-4P 193000-98-5P
     193000-99-6P 193001-00-2P 193001-01-3P
     193001-02-4P 193001-03-5P 193001-04-6P
     193001-06-8P 193001-09-1P 193001-14-8P
     193001-16-0P 193001-18-2P 193001-32-0P
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation and antiangiogenic and/or vascular permeability reducing effect
        of quinazoline derivs.)
RN
     192999-68-1 CAPLUS
     Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-
CN
    methyl-, hydrochloride (5:1) (9CI) (CA INDEX NAME)
```

## ●1/5 HCl

RN 192999-70-5 CAPLUS
CN Phenol, 5-[[6-methoxy-7-(3-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 192999-71-6 CAPLUS

CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, hydrochloride (4:3) (9CI) (CA INDEX NAME)

●3/4 HCl

RN 192999-72-7 CAPLUS

CN Phenol, 5-[[6-methoxy-7-(4-pyrimidinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 192999-73-8 CAPLUS

CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

## ●19/10 HCl

RN 192999-74-9 CAPLUS
CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4 quinazolinyl]amino]-2-methyl-, hydrochloride (10:17) (9CI) (CA INDEX NAME)

# ●17/10 HCl

RN 192999-75-0 CAPLUS
CN Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-76-1 CAPLUS

CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 192999-77-2 CAPLUS

CN Phenol, 5-[[7-[(3,5-dimethyl-4-isoxazolyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-78-3 CAPLUS
CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2methyl-, dihydrochloride (9CI) (CA INDEX NAME)

●2 HCl

RN 192999-79-4 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

## •2 HCl

RN 192999-80-7 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

## ●2 HCl

RN 192999-81-8 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-88-5 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]-2methyl- (9CI) (CA INDEX NAME)

RN 192999-89-6 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{S} \\ \end{array} \begin{array}{c} \text{CH}_2 - \text{O} \\ \text{MeO} \\ \end{array} \begin{array}{c} \text{N} \\ \text{N} \\ \text{N} \\ \end{array} \begin{array}{c} \text{NH} \\ \text{OH} \\ \end{array}$$

RN 192999-90-9 CAPLUS

CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 192999-94-3 CAPLUS

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-95-4 CAPLUS

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-96-5 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-98-7 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

●19/10 HCl

RN 192999-99-8 CAPLUS

CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

# ●19/10 HCl

RN 193000-00-9 CAPLUS
CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  OH  $\sim$  OH

## •2 HCl

RN 193000-01-0 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-02-1 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} S & CH_2 - O & N & N \\ \hline MeO & NH & NH & OH \\ \hline Me & Me & OH & NH \\ \hline \end{array}$$

● HCl

RN 193000-03-2 CAPLUS

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

HCl

RN 193000-10-1 CAPLUS
CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:19) (9CI) (CA
INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{N} \\ \text{C1} \\ \text{MeO} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{OH} \\ \text{Me} \\ \end{array}$$

●19/10 HCl

RN 193000-26-9 CAPLUS
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-27-0 CAPLUS
CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4-

n Phenol, 5-[[7-[(2-chioro-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, monohydrochloride (9CI) (CA INDEX
NAME)

HCl

RN 193000-39-4 CAPLUS

CN Phenol, 4-fluoro-2-methyl-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 193000-41-8 CAPLUS
CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4 quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:9) (9CI) (CA
 INDEX NAME)

$$\begin{array}{c|c} F & & \\ \hline \\ F & & \\ \hline \\ MeO & & \\ \hline \\ Me & \\ \hline \\ Me & \\ \hline \\ Me & \\ \hline \\ \\ OH & \\ \hline \\ \\ OH & \\ \hline \\ \\ OH & \\ \hline \\ \\ \end{array}$$

●9/10 HCl

RN 193000-42-9 CAPLUS
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 193000-43-0 CAPLUS

CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} Me \\ \hline \\ N \\ \hline \\ N \\ \end{array}$$
 
$$\begin{array}{c} CH_2 - O \\ \hline \\ N \\ \end{array}$$
 
$$\begin{array}{c} N \\ NH \\ \hline \\ OH \\ \end{array}$$

●9/5 HCl

RN 193000-44-1 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]-2-methyl-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

$$\begin{array}{c} N \\ N \\ \end{array} \begin{array}{c} CH_2 - CH_2 - O \\ \\ MeO \end{array} \begin{array}{c} N \\ NH \\ \end{array} \begin{array}{c} NH \\ \\ OH \\ \end{array}$$

●6/5 HCl

RN 193000-45-2 CAPLUS
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

HCl

RN 193000-46-3 CAPLUS
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-CH_2-O & N \\ \hline N & NH \\ \hline F & OH \\ \hline C1 & C1 \\ \end{array}$$

●9/5 HCl

RN 193000-47-4 CAPLUS
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

## ●6/5 HCl

RN 193000-59-8 CAPLUS

CN Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

## ●19/10 HCl

RN 193000-76-9 CAPLUS

CN Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-77-0 CAPLUS

CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-78-1 CAPLUS

CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-79-2 CAPLUS

CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-80-5 CAPLUS

CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-81-6 CAPLUS

CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-82-7 CAPLUS

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ & & & \\ NH & & \\ \hline & & \\ NH & & \\ \hline & & \\ NH & & \\ \end{array}$$

RN 193000-83-8 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-O & N & N \\ \hline N & NH & NH \\ \hline Me & OH \\ \end{array}$$

RN 193000-84-9 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

RN 193000-85-0 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{S} \\ \end{array} \begin{array}{c} \text{CH}_2 - \text{O} \\ \text{MeO} \\ \end{array} \begin{array}{c} \text{N} \\ \text{N} \\ \text{N} \\ \text{OH} \\ \end{array}$$

RN 193000-86-1 CAPLUS CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-O & & N \\ \hline & N \\ \hline & NH \\ \hline & NH \\ \hline & OH \\ \hline & Me \\ \end{array}$$

RN 193000-87-2 CAPLUS
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-88-3 CAPLUS

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{AcNH} & \text{N} & \text{CH}_2 - \text{O} & \text{N} \\ & \text{MeO} & \text{NH} & \text{NH} \\ & & \text{OH} & \text{Me} \\ \end{array}$$

RN 193000-89-4 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]- (9CI) (CA INDEX NAME)

RN 193000-90-7 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193000-91-8 CAPLUS

CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$ 

RN 193000-92-9 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193000-93-0 CAPLUS

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-94-1 CAPLUS

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

RN 193000-96-3 CAPLUS

CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-97-4 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193000-98-5 CAPLUS

CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Cl} \\ \text{N} \\ \text{MeO} \\ \end{array}$$

RN 193000-99-6 CAPLUS

CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} F & & \\ \hline \\ F & & \\ \hline \\ MeO & & \\ \hline \\ Me & \\ \hline \\ Me & \\ \end{array}$$

RN 193001-00-2 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-01-3 CAPLUS
CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-02-4 CAPLUS
CN Phenol, 4-fluoro-2-methyl-5-[[7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-03-5 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-04-6 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-06-8 CAPLUS

CN Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

RN 193001-09-1 CAPLUS

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 193001-14-8 CAPLUS

CN Phenol, 4-fluoro-2-methyl-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino]-(9CI) (CA INDEX NAME)

RN 193001-16-0 CAPLUS

CN Phenol, 2-chloro-4-fluoro-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino]-(9CI) (CA INDEX NAME)

193001-18-2 CAPLUS RN

Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN193001-32-0 CAPLUS

Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-CN (9CI) (CA INDEX NAME)

$$N - CH_2 - CH_2 - O$$

$$MeO$$

$$NH$$

$$NH$$

L24 ANSWER 9 OF 15 USPATFULL on STN

DUPLICATE 3

ACCESSION NUMBER:

2002:55045 USPATFULL

TITLE: INVENTOR(S): Chemical compounds

Lohmann, Jean-Jacques Marcel, Merfy, FRANCE Hennequin, Laurent Francois Andre, Champigny sur

Vesles, FRANCE

MIMPED

Thomas, Andrew Peter, Congleton, UNITED KINGDOM

filed on 17 Dec 1996, GRANTED, Pat. No. US 5962458

חאתב

KIND

PATENT ASSIGNEE(S): ZENECA LIMITED (non-U.S. corporation)

	NUMBER	KIND	DAIE	
PATENT INFORMATION:	US 2002032208	A1	20020314	
	US 6362336	B2	20020326	
APPLICATION INFO.:	US 2001-877005	<b>A</b> 1	20010611	(9)
RELATED APPLN. INFO.:	Division of Ser.	No. US	2000-5004	70, filed on 9 Feb
	2000, GRANTED, P	at. No.	US 625895	1 Continuation of Ser.
	No. US 1998-2037	64, file	ed on 2 De	c 1998, GRANTED, Pat.
	No. US 6071921 C	ontinua	tion of Se	r. No. US 1996-768887,

```
DATE
                              NUMBER
                        _____
PRIORITY INFORMATION:
                       EP 1995-402846
                                         19951218
                       EP 1996-402190
                                         19961015
DOCUMENT TYPE:
                       Utility
FILE SEGMENT:
                       APPLICATION
LEGAL REPRESENTATIVE:
                       Pillsbury Winthrop LLP, Intellectual Property Group,
                       East Tower, Ninth Floor, 1100 New York Avenue, N.W.,
                        Washington, DC, 20005-3918
NUMBER OF CLAIMS:
EXEMPLARY CLAIM:
LINE COUNT:
                        5568
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention relates to quinazoline derivatives of the formula:
       ##STR1##
       [wherein:
       Y.sup.1 represents --O--, --S--, --CH.sub.2--, --SO--, --SO.sub.2--,
       --NR.sup.5CO--, --CONR.sup.6--, --SO.sub.2NR.sup.7--,
       --NR.sup.8SO.sub.2-- or --NR.sup.9-- (wherein R.sup.5, R.sup.6, R.sup.7,
       R.sup.8 and R.sup.9 each independently represents hydrogen, alkyl or
       alkoxyalkyl);
       R.sup.1 represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl,
       cyano, alkyl, alkoxy, alkylthio, amino or alkylamino.
       R.sup.2 represents hydrogen, hydroxy, halogeno, alkyl, alkoxy,
       trifluoromethyl, cyano, amino or nitro;
       m is an integer from 1 to 5;
       R.sup.3 represents hydroxy, halogeno, alkyl, alkoxy, alkanoyloxy,
       trifluoromethyl, cyano, amino or nitro;
       R.sup.4 represents a group which is or which contains an optionally
       substituted pyridone, phenyl or aromatic heterocyclic group] and salts
       thereof; processes for their preparation and pharmaceutical compositions
       containing a compound of formula I or a pharmaceutically acceptable salt
       thereof as active ingredient.
       The compounds of formula I and the pharmaceutically acceptable salts
       thereof inhibit the effects of VEGF, a property of value in the
       treatment of a number of disease states including cancer and rheumatoid
       arthritis.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 192999-68-1P 192999-70-5P 192999-71-6P
      192999-72-7P 192999-73-8P 192999-74-9P
      192999-75-0P 192999-76-1P 192999-77-2P
      192999-78-3P 192999-79-4P 192999-80-7P
      192999-81-8P 192999-88-5P 192999-89-6P
      192999-90-9P 192999-94-3P 192999-95-4P
      192999-96-5P 192999-98-7P 192999-99-8P
      193000-00-9P 193000-01-0P 193000-02-1P
      193000-03-2P 193000-10-1P 193000-26-9P
      193000-27-0P 193000-39-4P 193000-40-7P
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193000-41-8P 193000-42-9P 193000-43-0P 193000-44-1P 193000-45-2P 193000-46-3P

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193000-47-4P 193000-59-8P 193000-76-9P
     193000-77-0P 193000-78-1P 193000-79-2P
     193000-80-5P 193000-81-6P 193000-82-7P
     193000-83-8P 193000-84-9P 193000-85-0P
     193000-86-1P 193000-87-2P 193000-88-3P
     193000-89-4P 193000-90-7P 193000-91-8P
     193000-92-9P 193000-93-0P 193000-94-1P
     193000-96-3P 193000-97-4P 193000-98-5P
     193000-99-6P 193001-00-2P 193001-01-3P
     193001-02-4P 193001-03-5P 193001-04-6P
     193001-06-8P 193001-09-1P 193001-14-8P
     193001-16-0P 193001-18-2P 193001-32-0P
        (preparation and antiangiogenic and/or vascular permeability reducing effect
       of quinazoline derivs.)
     192999-68-1 USPATFULL
RN
    Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-
CN
      methyl-, hydrochloride (5:1) (9CI) (CA INDEX NAME)
```

### ●1/5 HCl

RN 192999-71-6 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, hydrochloride (4:3) (9CI) (CA INDEX NAME)

●3/4 HCl

RN 192999-72-7 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(4-pyrimidinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 192999-73-8 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX

●19/10 HCl

RN 192999-74-9 USPATFULL
CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:17) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{CH}_2 - \text{O} & \text{N} \\ & \text{Me} & \text{N} & \text{N} \\ & & \text{HO} & \text{Me} \\ \end{array}$$

●17/10 HCl

RN 192999-76-1 USPATFULL

CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]-, dihydrochloride (9CI) (CA INDEX NAME)

●2 HCl

RN 192999-77-2 USPATFULL

CN Phenol, 5-[[7-[(3,5-dimethyl-4-isoxazolyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

#### HCl

RN 192999-78-3 USPATFULL CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2methyl-, dihydrochloride (9CI) (CA INDEX NAME)

### •2 HCl

RN 192999-79-4 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

#### •2 HCl

RN 192999-80-7 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ N & & & \\ & & & \\ Me & & \\ \end{array}$$

### ●2 HCl

RN 192999-81-8 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-88-5 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]-2methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Ph-CH}_2-\text{O} & \text{N} \\ & \text{MeO} & \text{N} \\ & \text{O} & \\ & \text{Me} & \text{OH} \end{array}$$

RN 192999-89-6 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{S} \\ \end{array} \begin{array}{c} \text{CH}_2 - \text{O} \\ \text{Me} \\ \end{array} \begin{array}{c} \text{N} \\ \text{N} \\ \text{N} \\ \end{array}$$

RN 192999-90-9 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-O & N & N \\ \hline NN & NH & NH \\ \hline F & OH & Me \\ \end{array}$$

●2 HCl

RN 192999-94-3 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-95-4 USPATFULL

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-96-5 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-98-7 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

●19/10 HCl

RN 192999-99-8 USPATFULL CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

$$N \longrightarrow CH_2 - CH_2 - O \longrightarrow N$$
 $MeO \longrightarrow N$ 
 $N \longrightarrow N$ 

## ●19/10 HCl

RN 193000-00-9 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

# ●2 HCl

RN 193000-01-0 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-02-1 USPATFULL

Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-CN 2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN

193000-03-2 USPATFULL
Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-CN7-quinazolinyl]oxy]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-10-1 USPATFULL CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{CH}_2-\text{O} & \text{N} \\ \text{N} & \text{MeO} & \text{N} \\ \text{C1} & \text{NH} & \text{OH} \\ \end{array}$$

●19/10 HCl

RN 193000-26-9 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-27-0 USPATFULL
CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, monohydrochloride (9CI) (CA
INDEX NAME)

$$\begin{array}{c} \text{C1} \\ \text{N} \\ \text{MeO} \end{array} \begin{array}{c} \text{N} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{OH} \end{array}$$

● HCl

● HCl

RN 193000-41-8 USPATFULL
CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:9) (9CI) (CA
INDEX NAME)

$$\begin{array}{c} \text{F} \\ \text{MeO} \\ \text{NH} \\ \text{NH} \\ \text{OH} \\ \text{Me} \\ \end{array}$$

●9/10 HCl

RN 193000-42-9 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

●2 HCl

RN 193000-43-0 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

●9/5 HCl

RN 193000-44-1 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4quinazolinyl]amino]-2-methyl-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

●6/5 HCl

RN 193000-45-2 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-46-3 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{CH}_2\text{-CH}_2\text{-O} & \text{N} \\ \text{MeO} & \text{N} \\ \end{array}$$

●9/5 HCl

RN 193000-47-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

## ●6/5 HCl

RN 193000-59-8 USPATFULL CN Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

#### ●19/10 HCl

RN 193000-76-9 USPATFULL CN Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

RN 193000-77-0 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-78-1 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-79-2 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{Me} \\ \text{O} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{Me} \\ \\ \text{N} \\ \text{Me} \\ \\ \text{N} \\ \text$$

RN 193000-80-5 USPATFULL

CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-81-6 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ \hline & & & \\ N & & \\ MeO & & \\ \hline & & & \\ NH & & \\ Me & & \\ \end{array}$$

RN 193000-82-7 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-83-8 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-84-9 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

RN 193000-85-0 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-86-1 USPATFULL CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ \hline & & & \\ N & & & \\ \hline & & & \\ N & & & \\ N & & \\ N & & \\ \hline & & \\ N & & \\ N & & \\ \end{array}$$

RN 193000-87-2 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-88-3 USPATFULL

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-89-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]- (9CI) (CA INDEX NAME)

RN 193000-90-7 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ N & & & \\ N & & & \\ N & & \\ MeO & & & \\ NH & & \\ NH & & \\ OH & & \\ C1 & & \\ \end{array}$$

RN 193000-91-8 USPATFULL

CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-92-9 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

N— 
$$CH_2$$
—  $CH_2$ —  $OH_2$ —  $O$ 

RN 193000-93-0 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ & & & \\ N & & \\ MeO & & \\ & & \\ NH & & \\$$

RN 193000-94-1 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

RN 193000-96-3 USPATFULL

CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{N} \\ \text{N} & \text{N} & \text{N} \\ \text{C1} & \text{NH} & \text{NH} \\ & \text{Me} & \text{OH} \end{array}$$

RN 193000-97-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ & & & \\ NH & & \\ & & & \\ NH & & \\ & & & \\ NH & & \\ & & & \\ OH & & \\ \end{array}$$

RN 193000-98-5 USPATFULL

CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-99-6 USPATFULL

CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} F \\ \hline \\ CH_2-O \\ \hline \\ MeO \\ \hline \\ NH \\ \hline \\ NH \\ \hline \\ OH \\ \\ Me \\ \end{array}$$

RN 193001-00-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-01-3 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-02-4 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} N \\ N \\ \end{array} \begin{array}{c} N \\ \end{array} \begin{array}{c} CH_2 - CH_2 - O \\ \end{array} \begin{array}{c} N \\ NH \\ \end{array} \begin{array}{c} NH \\ \end{array} \begin{array}{c} NH \\ \end{array} \begin{array}{c} OH \\$$

RN 193001-03-5 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-04-6 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{CH}_2\text{-CH}_2\text{-O} \\ & \text{MeO} \end{array}$$

RN 193001-06-8 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

RN 193001-09-1 USPATFULL

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 193001-14-8 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

RN 193001-16-0 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

RN 193001-18-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{CH}_2 - \text{O} & \text{N} & \text{N} \\ & & \text{MeO} & & \text{NH} & \\ & & & \text{OH} & \\ & & & \text{OH} & \\ \end{array}$$

RN 193001-32-0 USPATFULL

CN Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

PRIORITY INFORMATION:

L24 ANSWER 10 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2002:290948 USPATFULL

TITLE: Processes and intermediates for preparing anti-cancer

compounds

INVENTOR(S): Norris, Timothy, Gales Ferry, CT, United States

Santafianos, Dinos P., Groton, CT, United States Lehner, Richard S., Ledyard, CT, United States

PATENT ASSIGNEE(S): Pfizer Inc., New York, NY, United States (U.S.

corporation)

Pfizer Products Inc., Groton, CT, United States (U.S.

19990331 (60)

corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION: APPLICATION INFO.:	US 6476040 US 2000-538635	B1	20021105	(9)
	NUMBER DATE			

US 1999-127072P

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: Truong, Tamthom N.
LEGAL REPRESENTATIVE: Ladas & Parry

NUMBER OF CLAIMS: 17 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)

LINE COUNT: 945

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods and intermediates for preparing compounds of the formula 1 ##STR1##

and the pharmaceutically acceptable salts and solvates thereof, as well as structurally related compounds, wherein R.sup.1, R.sup.2 and R.sup.15 are as defined herein. The foregoing compounds are useful in the treatment of hyperproliferative disorders, such as cancers, in mammals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 299912-65-5P

(method for preparation of anticancer (ethynylphenylamino)quinazoline derivs. and intermediates thereof)

RN 299912-65-5 USPATFULL

CN 4-Quinazolinamine, 6-(2-methoxyethoxy)-N-(4-methoxyphenyl)-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Ph-CH}_2\text{-O} \\ \text{MeO-CH}_2\text{-CH}_2\text{-O} \\ \end{array}$$

L24 ANSWER 11 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2001:158278 USPATFULL

TITLE: 4-anilinoquinazoline derivatives

INVENTOR(S): Thomas, Andrew Peter, Macclesfield, United Kingdom

Johnstone, Craig, Macclesfield, United Kingdom

Hennequin, Laurent Francois Andre, Reims Cedex, France

PATENT ASSIGNEE(S): Zeneca Limited, London, United Kingdom (non-U.S.

corporation)

Zeneca Pharma S.A., Cergy Cedex, France (non-U.S.

corporation)

 WO 1997-GB550

19970228

19980908 PCT 371 date 19980908 PCT 102(e) date

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Raymond, Richard L.

ASSISTANT EXAMINER: Balasubramanian, Venkataraman

LEGAL REPRESENTATIVE: Pillsbury Winthrop LLP

NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 2457

AΒ

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to quinazoline derivatives of formula (I) (wherein: R.sup.1 represents hydrogen or methoxy; R.sup.2 represents methoxy, ethoxy, 2-methoxyethoxy, 3-methoxypropoxy, 2-ethoxyethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy, 2-hydroxyethoxy, 3-hydroxypropoxy, 2-(N,N-dimethylamino)ethoxy, 3-(N,Ndimethylamino)propoxy, 2-morpholinoethoxy, 3-morpholinopropoxy, 4-morpholinobutoxy, 2-piperidinoethoxy, 3-piperidinopropoxy, 4-piperidinobutoxy, 2-(piperazin-1-yl)ethoxy, 3-(piperazin-1-yl)propoxy, 4-(piperazin-1-yl)butoxy, 2-(4-methylpiperazin-1-yl)ethoxy, 3-(4methylpiperazin-1-yl)propoxy or 4-(4-methylpiperazin-1-yl)butoxy; the phenyl group bearing (R.sup.3).sub.2 is selected from: 2-fluoro-5-hydroxyphenyl, 4-bromo-2-fluorophenyl, 2,4-difluorophenyl, 4-chloro-2-fluorophenyl, 2-fluoro-4-methylphenyl, 2-fluoro-4methoxyphenyl, 4-bromo-3-hydroxyphenyl, 4-fluoro-3-hydroxyphenyl, 4-chloro-3-hydroxyphenyl, 3-hydroxy-4-methylphenyl, 3-hydroxy-4methoxyphenyl and 4-cyano-2-fluorophenyl); and salts thereof, processes for their preparation and pharmaceutical compositions containing a compound of formula (I) or a pharmaceutically acceptable salt thereof as active ingredient The compounds of formula (I) and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 196603-79-9P

(preparation of 4-anilinoquinazolines for use in the treatment of disease states associated with antiangiogenesis and/or increased vascular permeability)

RN 196603-79-9 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

L24 ANSWER 12 OF 15 USPATFULL on STN

2001:108033 USPATFULL ACCESSION NUMBER: Chemical compounds TITLE:

Lohmann, Jean-Jacques Marcel, Merfy, France INVENTOR (S):

Hennequin, Laurent Francois Andre, Champigny sur

Vesles, France

Thomas, Andrew Peter, Congleton, United Kingdom Zeneca Limited, London, United Kingdom (non-U.S. PATENT ASSIGNEE(S):

corporation)

Zeneca Pharma S.A., Cergy Cedex, France (non-U.S.

corporation)

NUMBER KIND DATE .\_\_\_\_\_ \_\_\_\_ PATENT INFORMATION: US 6258951 20010710 B1 APPLICATION INFO.: US 2000-500470 20000209 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-203764, filed on 2 Dec 1998 Continuation of Ser. No. US 1996-768887, filed on

17 Dec 1996, now patented, Pat. No. US 5962458

NUMBER DATE EP 1995-402846 PRIORITY INFORMATION: 19951218 EP 1996-402190 19961015

DOCUMENT TYPE: Utility GRANTED FILE SEGMENT: PRIMARY EXAMINER: Kifle, Bruck

LEGAL REPRESENTATIVE: Pillsbury Winthrop LLP

NUMBER OF CLAIMS: EXEMPLARY CLAIM: LINE COUNT: 5180

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to quinazoline derivatives of the formula:

##STR1##

and salts thereof; processes for their preparation and pharmaceutical compositions containing a compound of formula I or a pharmaceutically acceptable salt thereof as active ingredient.

The compounds of formula I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 192999-68-1P 192999-70-5P 192999-71-6P
     192999-72-7P 192999-73-8P 192999-74-9P
     192999-75-0P 192999-76-1P 192999-77-2P
     192999-78-3P 192999-79-4P 192999-80-7P
     192999-81-8P 192999-88-5P 192999-89-6P
     192999-90-9P 192999-94-3P 192999-95-4P
     192999-96-5P 192999-98-7P 192999-99-8P
     193000-00-9P 193000-01-0P 193000-02-1P
     193000-03-2P 193000-10-1P 193000-26-9P
     193000-27-0P 193000-39-4P 193000-40-7P
     193000-41-8P 193000-42-9P 193000-43-0P
     193000-44-1P 193000-45-2P 193000-46-3P
     193000-47-4P 193000-59-8P 193000-76-9P
     193000-77-0P 193000-78-1P 193000-79-2P
     193000-80-5P 193000-81-6P 193000-82-7P
     193000-83-8P 193000-84-9P 193000-85-0P
     193000-86-1P 193000-87-2P 193000-88-3P
     193000-89-4P 193000-90-7P 193000-91-8P
     193000-92-9P 193000-93-0P 193000-94-1P
     193000-96-3P 193000-97-4P 193000-98-5P
     193000-99-6P 193001-00-2P 193001-01-3P
     193001-02-4P 193001-03-5P 193001-04-6P
     193001-06-8P 193001-09-1P 193001-14-8P
     193001-16-0P 193001-18-2P 193001-32-0P
        (preparation and antiangiogenic and/or vascular permeability reducing effect
       of quinazoline derivs.)
RN
    192999-68-1 USPATFULL
    Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-
CN
      methyl-, hydrochloride (5:1) (9CI) (CA INDEX NAME)
```

●1/5 HCl

RN 192999-70-5 USPATFULL
CN Phenol, 5-[[6-methoxy-7-(3-pyridinylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

192999-71-6 USPATFULL RN

Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, hydrochloride (4:3) (9CI) (CA INDEX NAME) CN

●3/4 HCl

192999-72-7 USPATFULL RN

Phenol, 5-[[6-methoxy-7-(4-pyrimidinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME) CN

RN 192999-73-8 USPATFULL
CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

●19/10 HCl

RN 192999-74-9 USPATFULL
CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:17) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{CH}_2-\text{O} & \text{N} & \text{N} \\ & & \text{MeO} & & \text{NH} \\ & & & \text{HO} & & \text{Me} \\ \end{array}$$

●17/10 HCl

RN 192999-75-0 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-76-1 USPATFULL

CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]-, dihydrochloride (9CI) (CA INDEX NAME)

#### •2 HCl

RN 192999-77-2 USPATFULL
CN Phenol, 5-[[7-[(3,5-dimethyl-4-isoxazolyl)methoxy]-6-methoxy-4quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

#### ● HCl

RN 192999-78-3 USPATFULL CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2methyl-, dihydrochloride (9CI) (CA INDEX NAME)

#### •2 HCl

RN 192999-79-4 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

## •2 HCl

RN 192999-80-7 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

●2 HCl

RN 192999-81-8 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-88-5 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]-2-methyl- (9CI) (CA INDEX NAME)

RN 192999-89-6 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{S} \\ \end{array}$$

● HCl

RN 192999-90-9 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 192999-94-3 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-95-4 USPATFULL

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-96-5 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-98-7 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

#### ●19/10 HCl

RN 192999-99-8 USPATFULL CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

N— 
$$CH_2$$
—  $CH_2$ —  $OH_2$ —  $O$ 

# ●19/10 HCl

RN 193000-00-9 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  OH  $\sim$  OH

#### •2 HCl

RN 193000-01-0 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

#### HCl

RN 193000-02-1 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 193000-03-2 USPATFULL

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 193000-10-1 USPATFULL

CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{N} \\ \text{N} & \text{N} & \text{N} \\ \text{C1} & \text{NH} & \text{NH} \\ & \text{Me} & \text{OH} \\ \end{array}$$

## ●19/10 HCl

RN 193000-26-9 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

## ● HCl

RN 193000-27-0 USPATFULL CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{C1} \\ \text{N} \\ \text{N} \\ \text{MeO} \\ \end{array}$$

● HCl

● HCl

● HCl

RN 193000-41-8 USPATFULL CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:9) (9CI) (CA INDEX NAME)

$$\begin{array}{c} F \\ F \\ \end{array} \begin{array}{c} CH_2 - O \\ \\ MeO \\ \end{array} \begin{array}{c} N \\ NH \\ \\ Me \\ \end{array} \begin{array}{c} OH \\ \end{array}$$

●9/10 HCl

RN 193000-42-9 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 193000-43-0 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

●9/5 HCl

RN 193000-44-1 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]-2-methyl-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

## ●6/5 HCl

RN 193000-45-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

## ● HCl

RN 193000-46-3 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

### ●9/5 HCl

RN 193000-47-4 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{CH}_2 - \text{O} & \text{N} & \text{N} \\ & \text{MeO} & & \text{NH} & \text{NH} \\ & & & \text{OH} & & \text{OH} \\ \end{array}$$

#### ●6/5 HCl

RN 193000-59-8 USPATFULL

CN Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

#### ●19/10 HCl

RN 193000-76-9 USPATFULL
CN Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2 methyl- (9CI) (CA INDEX NAME)

RN 193000-77-0 USPATFULL CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

RN 193000-78-1 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-79-2 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{CH}_2 - \text{O} & \text{N} & \text{N} \\ & & \text{Me} & \text{O} & \text{N} & \text{N} \\ & & & \text{N} & \text{N} & \text{N} \\ & & & & \text{Me} & \text{N} \\ & & & & \text{Me} & \text{N} \end{array}$$

RN 193000-80-5 USPATFULL

CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-81-6 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{(CH}_2\text{)}_3\text{-0} \\ \text{MeO} \end{array}$$

RN 193000-82-7 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ N & & & \\ & & & \\ NH & & \\ \hline NH & & \\ N$$

RN 193000-83-8 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ & & & \\ NH & & \\ \hline & & \\ NH & & \\ \hline & & \\ NH & & \\ \hline & & \\ OH & & \\ \end{array}$$

RN 193000-84-9 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-85-0 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-86-1 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-O & N & N \\ \hline NN & NH & \\ \hline F & OH & \\ \hline Me & \end{array}$$

RN 193000-87-2 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-88-3 USPATFULL

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-89-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Ph-CH}_2\text{-0} & \text{N} \\ \text{MeO} & \text{N} \\ \end{array}$$

RN 193000-90-7 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193000-91-8 USPATFULL

CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  OH  $\sim$  NH  $\sim$  OH

RN 193000-92-9 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  OH  $\sim$  OH

RN 193000-93-0 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-CH_2-O & N \\ \hline N & N \\ \hline NH & \\ \hline F & OH \\ \hline Me & \\ \end{array}$$

RN 193000-94-1 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]2-methyl- (9CI) (CA INDEX NAME)

RN 193000-96-3 USPATFULL CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{N} \\ \text{Cl} \\ \text{MeO} \\ \text{NH} \\ \text{NH} \\ \text{OH} \\ \text{OH} \\ \end{array}$$

RN 193000-97-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193000-98-5 USPATFULL

CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-99-6 USPATFULL

CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4-

quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

RN 193001-00-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} Me \\ \hline \\ N \\ \hline \\ N \\ \hline \\ MeO \\ \hline \\ NH \\ \hline \\ NH \\ \hline \\ OH \\ \hline \\ C1 \\ \end{array}$$

RN 193001-01-3 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-02-4 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-03-5 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-04-6 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-

quinazolinyl]amino] - (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-CH_2-O & N \\ \hline N & N \\ \hline NH & NH \\ \hline C1 & OH \\ \end{array}$$

RN 193001-06-8 USPATFULL CN Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

RN 193001-09-1 USPATFULL

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

RN 193001-14-8 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

RN 193001-16-0 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

RN 193001-18-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-32-0 USPATFULL

Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-CN (9CI) (CA INDEX NAME)

L24 ANSWER 13 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2001:18472 USPATFULL

Quinazoline derivatives as VEGF inhibitors TITLE:

Thomas, Andrew Peter, Macclesfield, United Kingdom INVENTOR(S):

Johnstone, Craig, Macclesfield, United Kingdom

Hennequin, Laurent Francois Andre, Reims Cedex, France

PATENT ASSIGNEE(S): Zeneca Limited, London, United Kingdom (non-U.S.

corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6184225	B1	20010206	
	WO 9730035		19970821	
APPLICATION INFO.:	US 1998-125271		19980813	(9)
	WO 1997-GB365		19970210	
			19980813	PCT 371 date
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PRIORITY	INFORMATION:	EP 1996-400293 EP 1996-401756	19960213 19960808
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Raymond, Richard L. PRIMARY EXAMINER: ASSISTANT EXAMINER: Schroeder, Ben

Pillsbury Madison & Sutro LLPIntellectual Property LEGAL REPRESENTATIVE:

Group

NUMBER OF CLAIMS: 18 EXEMPLARY CLAIM: LINE COUNT: 3619

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to quinazoline derivatives of formula (I) ##STR1##

wherein: Z represents --O--, --NH-- or --S--; m is an integer from 1 to 5; R.sup.1 represents hydrogen, hydroxy, halogeno, nitro, trifluorometlyl, cyano, C.sub.1-3 alkyl, C.sub.1-3 alkoxy, C.sub.1-3 alkylthio or NR.sup.5 R.sup.6 (wherein R.sup.5 and R.sup.6, which may be the same or different, each represents hydrogen or C.sub.1-3 alkyl);

R.sup.2 represents hydrogen, hydroxy, halogeno, methoxy, amino, or nitro; R.sup.3 represents hydroxy, halogeno, C.sub.1-3 alkyl, C.sub.1-3 alkoxy, C.sub.1-3 alkanoyloxy, trifluoromethyl, cyano, amino or nitro; X.sup.1 represents --O--, --CH.sub.2 --, --S--, --SO--, SO.sub.2 --, --NR.sup.6 --, NR.sup.8 CO--, --CONR.sup.9 --SO.sub.2 NR.sup.10 -- or --NR.sup.11 SO.sub.2 --, (wherein R.sup.7, R.sup.8, R.sup.9, R.sup.10 and R.sup.11 each represents C.sub.1-3 alkyl, C.sub.1-3 alkoxyC.sub.2-3 alkyl); R.sup.4 represents a group which is alkenyl, alkynyl or optionally substituted alkyl, which alkyl group may contain a heteroatom linking group, which alkenyl, alkynyl or alkyl group may carry a terminal optionally substituted 5 or 6 membered saturated carbocylic or heterocyclic group; and salts thereof, processes for their preparation, pharmaceutical compositions containing a compound of formula (I) or a pharmaceutically acceptable salt thereof as active ingredient the compounds of formula (I) and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 192999-96-5P

(preparation of quinazolines as VEGF inhibitors)

RN 192999-96-5 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

HCl

L24 ANSWER 14 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2000:70850 USPATFULL

TITLE:

Chemical compounds

INVENTOR(S):

Lohmann, Jean-Jacques Marcel, Merfy, France

Hennequin, Laurent Francois Andre, Champigny sur

Vesles, France

Thomas, Andrew Peter, Congleton, United Kingdom

PATENT ASSIGNEE(S):

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corporation)

Zeneca Pharma S.A., Cergy Cedex, France (non-U.S.

corporation)

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NUMBER DATE

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PRIMARY EXAMINER: Shah, Mukund J. ASSISTANT EXAMINER: Kifle, Bruck

LEGAL REPRESENTATIVE: Pillsbury Madison & Sutro, LLP Intellectual Property

Group

NUMBER OF CLAIMS: 13 EXEMPLARY CLAIM: 1 LINE COUNT: 5709

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to quinazoline derivatives of the formula:

##STR1## [wherein: Y.sup.1 represents --O--, --S--, --CH.sub.2 --,
--SO--, --SO.sub.2 --, --NR.sup.5 CO--, --CONR.sup.6 --, --SO.sub.2

NR.sup.7 --, --NR.sup.8 SO.sub.2 -- or --NR.sup.9 -- (wherein R.sup.5,
R.sup.6, R.sup.7, R.sup.8 and R.sup.9 each independently represents
hydrogen, alkyl or alkoxyalkyl);

R.sup.1 represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, alkyl, alkoxy, alkylthio, amino or alkylamino.

R.sup.2 represents hydrogen, hydroxy, halogeno, alkyl, alkoxy, trifluoromethyl, cyano, amino or nitro;

m is an integer from 1 to 5;

R.sup.3 represents hydroxy, halogeno, alky, alkoxy, alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

R.sup.4 represents a group which is or which contains an optionally substituted pyridone, phenyl or aromatic heterocyclic group] and salts thereof; processes for their preparation and pharmaceutical compositions containing a compound of formula I or a pharmaceutically acceptable salt thereof as active ingredient.

The compounds of formula I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 192999-68-1P 192999-70-5P 192999-71-6P

192999-72-7P 192999-73-8P 192999-74-9P

192999-75-0P 192999-76-1P 192999-77-2P

192999-78-3P 192999-79-4P 192999-80-7P

192999-81-8P 192999-88-5P 192999-89-6P

192999-90-9P 192999-94-3P 192999-95-4P

192999-96-5P 192999-98-7P 192999-99-8P

193000-00-9P 193000-01-0P 193000-02-1P

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193000-03-2P 193000-10-1P 193000-26-9P
     193000-27-0P 193000-39-4P 193000-40-7P
     193000-41-8P 193000-42-9P 193000-43-0P
     193000-44-1P 193000-45-2P 193000-46-3P
     193000-47-4P 193000-59-8P 193000-76-9P
     193000-77-0P 193000-78-1P 193000-79-2P
     193000-80-5P 193000-81-6P 193000-82-7P
     193000-83-8P 193000-84-9P 193000-85-0P
     193000-86-1P 193000-87-2P 193000-88-3P
     193000-89-4P 193000-90-7P 193000-91-8P
     193000-92-9P 193000-93-0P 193000-94-1P
     193000-96-3P 193000-97-4P 193000-98-5P
     193000-99-6P 193001-00-2P 193001-01-3P
     193001-02-4P 193001-03-5P 193001-04-6P
     193001-06-8P 193001-09-1P 193001-14-8P
     193001-16-0P 193001-18-2P 193001-32-0P
        (preparation and antiangiogenic and/or vascular permeability reducing effect
       of quinazoline derivs.)
RN
     192999-68-1 USPATFULL
    Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-
CN
       methyl-, hydrochloride (5:1) (9CI) (CA INDEX NAME)
```

# ●1/5 HCl

```
RN 192999-70-5 USPATFULL
CN Phenol, 5-[[6-methoxy-7-(3-pyridinylmethoxy)-4-quinazolinyl]amino]-2-
methyl- (9CI) (CA INDEX NAME)
```

RN 192999-71-6 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, hydrochloride (4:3) (9CI) (CA INDEX NAME)

●3/4 HCl

RN 192999-72-7 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(4-pyrimidinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 192999-73-8 USPATFULL
CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX
NAME)

●19/10 HCl

RN 192999-74-9 USPATFULL CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:17) (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{S} \\ \end{array} \begin{array}{c} \text{CH}_2 - \text{O} \\ \text{MeO} \\ \end{array} \begin{array}{c} \text{N} \\ \text{NH} \\ \\ \text{Me} \\ \end{array}$$

●17/10 HCl

RN 192999-75-0 USPATFULL Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME) CN

● HCl

RNCN

192999-76-1 USPATFULL Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7quinazolinyl]oxy]methyl]-2-thiazolyl]-, dihydrochloride (9CI) (CA INDEX NAME)

### •2 HCl

RN 192999-77-2 USPATFULL
CN Phenol, 5-[[7-[(3,5-dimethyl-4-isoxazolyl)methoxy]-6-methoxy-4quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

### ● HCl

RN 192999-78-3 USPATFULL
CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2methyl-, dihydrochloride (9CI) (CA INDEX NAME)

### ●2 HCl

RN 192999-79-4 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

### ●2 HCl

RN 192999-80-7 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 192999-81-8 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-88-5 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]-2-methyl- (9CI) (CA INDEX NAME)

RN 192999-89-6 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{S} \\ \end{array}$$

● HCl

RN 192999-90-9 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

#### ●2 HCl

RN 192999-94-3 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

### ● HCl

RN 192999-95-4 USPATFULL

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-96-5 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-98-7 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

### ●19/10 HCl

RN 192999-99-8 USPATFULL CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

### ●19/10 HCl

RN 193000-00-9 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  OH  $\sim$  OH

### ●2 HCl

RN 193000-01-0 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ & & & \\ MeO & & & \\ & & & \\ & & & \\ & & & \\ NH & & \\ & & & \\ NH & & \\ & & \\ & & \\ OH & & \\ \end{array}$$

### ● HCl

RN 193000-02-1 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 193000-03-2 USPATFULL

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

• HCl

RN 193000-10-1 USPATFULL

CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

## ●19/10 HCl

### ● HCl

RN 193000-27-0 USPATFULL
CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, monohydrochloride (9CI) (CA
INDEX NAME)

● HCl

HCl

● HCl

RN 193000-41-8 USPATFULL
CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:9) (9CI) (CA
INDEX NAME)

●9/10 HCl

RN 193000-42-9 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-y1)methoxy]-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

### ●2 HCl

RN 193000-43-0 USPATFULL CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

### ●9/5 HCl

RN 193000-44-1 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]-2-methyl-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

$$\begin{array}{c} N \\ N \\ \end{array} \begin{array}{c} N \\ \end{array} \begin{array}{c} CH_2 - CH_2 - O \\ \end{array} \begin{array}{c} N \\ MeO \end{array} \begin{array}{c} N \\ NH \\ \end{array} \begin{array}{c} NH \\ OH \\ \end{array} \begin{array}{c} NH \\ Me \\ \end{array} \begin{array}{c} OH \\ \end{array}$$

●6/5 HCl

RN 193000-45-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 193000-46-3 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

### ●9/5 HCl

RN 193000-47-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

## ●6/5 HCl

RN 193000-59-8 USPATFULL

CN Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  N  $\sim$ 

### ●19/10 HCl

RN 193000-76-9 USPATFULL CN Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

RN 193000-77-0 USPATFULL CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

RN 193000-78-1 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-79-2 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-80-5 USPATFULL

CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-81-6 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ & & & \\ N & & \\ MeO & & \\ & & \\ NH & & \\ Me & & \\ \end{array}$$

RN 193000-82-7 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-83-8 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ & & & \\ NH & & \\ \hline NH & & \\ & & \\ NH & & \\ \end{array}$$

RN 193000-84-9 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-85-0 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{S} \\ \end{array} \begin{array}{c} \text{CH}_2 - \text{O} \\ \text{Me} \\ \end{array} \begin{array}{c} \text{N} \\ \text{N} \\ \text{N} \\ \text{OH} \\ \end{array}$$

RN 193000-86-1 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-O & N & N \\ \hline N & N & N \\ \hline N & N & \\ \hline Me & OH \\ \end{array}$$

RN 193000-87-2 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \\ \text{N} \\ \\ \text{N} \\ \\ \text{MeO} \\ \\ \text{NH} \\ \\ \text{OH} \\ \\ \text{OH} \\ \\ \\$$

RN 193000-88-3 USPATFULL

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-89-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]- (9CI) (CA INDEX NAME)

RN 193000-90-7 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193000-91-8 USPATFULL

CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-92-9 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

N— 
$$CH_2$$
—  $CH_2$ —  $OH_2$ —  $O$ 

RN 193000-93-0 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{CH}_2\text{-CH}_2\text{-O} & \text{N} \\ \text{MeO} & \text{NH} \\ \end{array}$$

RN 193000-94-1 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-96-3 USPATFULL
CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{C1} \\ \text{MeO} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{OH} \\ \text{OH} \\ \end{array}$$

RN 193000-97-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193000-98-5 USPATFULL

CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-99-6 USPATFULL

CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4-

quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

RN 193001-00-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} Me \\ \hline \\ N \\ \hline \\ N \\ \hline \\ MeO \\ \hline \\ NH \\ \hline \\ NH \\ \hline \\ OH \\ \hline \\ C1 \\ \end{array}$$

RN 193001-01-3 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-02-4 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} N \\ N \\ \end{array} \begin{array}{c} CH_2 - CH_2 - O \\ \end{array} \begin{array}{c} N \\ NH \\ \end{array} \begin{array}{c} NH \\ \end{array} \begin{array}{c} NH \\ \end{array} \begin{array}{c} OH \\ \end{array} \begin{array}{c} OH \\ \end{array}$$

RN 193001-03-5 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-04-6 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-

quinazolinyl]amino] - (9CI) (CA INDEX NAME)

RN 193001-06-8 USPATFULL CN Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

RN 193001-09-1 USPATFULL

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & &$$

RN 193001-14-8 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

RN 193001-16-0 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino]-(9CI) (CA INDEX NAME)

RN 193001-18-2 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-32-0 USPATFULL

CN Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

L24 ANSWER 15 OF 15 USPATFULL on STN

ACCESSION NUMBER: 1999:121360 USPATFULL TITLE: Substituted quinazolines

INVENTOR(S): Lohmann, Jean-Jacques Marcel, Merfy, France

Hennequin, Laurent Francois Andre, Champigny sur

Vesles, France

Thomas, Andrew Peter, Congleton, United Kingdom

PATENT ASSIGNEE(S): Zeneca Limited, London, United Kingdom (non-U.S.

corporation)

Zeneca Pharma S.A.,, Cergy Cedex, France (non-U.S.

19961015

corporation)

NUMBER DATE
PRIORITY INFORMATION: EP 1995-402846 19951218

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Shah, Mukund J. ASSISTANT EXAMINER: Kifle, Bruck

LEGAL REPRESENTATIVE: Pillsbury Madison & Sutro

NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 5497

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to quinazoline derivatives of the formula:

##STR1## [wherein: Y.sup.1 represents --O--, --S--, --CH.sub.2 --,
--SO--, --SO.sub.2 --, --NR.sup.5 CO--, --CONR.sup.6 -, --SO.sub.2

NR.sup.7 -, --NR.sup.8 SO.sub.2 -- or --NR.sup.9 - (wherein R.sup.5,
R.sup.6, R.sup.7, R.sup.8 and R.sup.9 each independently represents hydrogen, alkyl or alkoxyalkyl);

R.sup.1 represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, alkyl, alkoxy, alkylthio, amino or alkylamino.

R.sup.2 represents hydrogen, hydroxy, halogeno, alkyl, alkoxy, trifluoromethyl, cyano, amino or nitro;

m is an integer from 1 to 5;

R.sup.3 represents hydroxy, halogeno, alkyl, alkoxy, alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

R.sup.4 represents a group which is or which contains an optionally substituted pyridone, phenyl or aromatic heterocyclic group] and salts thereof; processes for their preparation and pharmaceutical compositions containing a compound of formula I or a pharmaceutically acceptable salt thereof as active ingredient. The compounds of formula I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis.

```
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 192999-68-1P 192999-70-5P 192999-71-6P
      192999-72-7P 192999-73-8P 192999-74-9P
      192999-75-0P 192999-76-1P 192999-77-2P
      192999-78-3P 192999-79-4P 192999-80-7P
      192999-81-8P 192999-88-5P 192999-89-6P
      192999-90-9P 192999-94-3P 192999-95-4P
      192999-96-5P 192999-98-7P 192999-99-8P
      193000-00-9P 193000-01-0P 193000-02-1P
      193000-03-2P 193000-10-1P 193000-26-9P
      193000-27-0P 193000-39-4P 193000-40-7P
      193000-41-8P 193000-42-9P 193000-43-0P
      193000-44-1P 193000-45-2P 193000-46-3P
      193000-47-4P 193000-59-8P 193000-76-9P
      193000-77-0P 193000-78-1P 193000-79-2P
      193000-80-5P 193000-81-6P 193000-82-7P
      193000-83-8P 193000-84-9P 193000-85-0P
      193000-86-1P 193000-87-2P 193000-88-3P
      193000-89-4P 193000-90-7P 193000-91-8P
      193000-92-9P 193000-93-0P 193000-94-1P
      193000-96-3P 193000-97-4P 193000-98-5P
      193000-99-6P 193001-00-2P 193001-01-3P
      193001-02-4P 193001-03-5P 193001-04-6P
      193001-06-8P 193001-09-1P 193001-14-8P
      193001-16-0P 193001-18-2P 193001-32-0P
        (preparation and antiangiogenic and/or vascular permeability reducing effect
        of guinazoline derivs.)
     192999-68-1 USPATFULL
RN
     Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-
CN
       methyl-, hydrochloride (5:1) (9CI) (CA INDEX NAME)
```

●1/5 HCl

RN 192999-70-5 USPATFULL CN Phenol, 5-[[6-methoxy-7-(3-pyridinylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

RN 192999-71-6 USPATFULL CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2methyl-, hydrochloride (4:3) (9CI) (CA INDEX NAME)

●3/4 HCl

RN 192999-72-7 USPATFULL
CN Phenol, 5-[[6-methoxy-7-(4-pyrimidinylmethoxy)-4-quinazolinyl]amino]-2methyl- (9CI) (CA INDEX NAME)

## ●19/10 HCl

RN 192999-74-9 USPATFULL
CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:17) (9CI) (CA INDEX NAME)

## ●17/10 HCl

RN 192999-75-0 USPATFULL CN Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-76-1 USPATFULL
CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7quinazolinyl]oxy]methyl]-2-thiazolyl]-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 192999-77-2 USPATFULL CN Phenol, 5-[[7-[(3,5-dimethyl-4-isoxazolyl)methoxy]-6-methoxy-4quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 192999-79-4 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

RN 192999-80-7 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ \hline & & & \\ NH & & \\ \hline & & \\ NH & & \\ \hline & & \\ NH & & \\ \hline & & \\ OH & & \\ \end{array}$$

# •2 HCl

RN 192999-81-8 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-88-5 USPATFULL CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]-2methyl- (9CI) (CA INDEX NAME)

RN 192999-89-6 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-90-9 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 192999-94-3 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 192999-95-4 USPATFULL

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 192999-96-5 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

HCl

RN 192999-98-7 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

●19/10 HCl

RN 192999-99-8 USPATFULL
CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4quinazolinyl]amino]-2-methyl-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  OH  $\sim$  NH  $\sim$  OH

## ●19/10 HCl

RN 193000-00-9 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

## •2 HCl

RN 193000-01-0 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-02-1 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 193000-03-2 USPATFULL

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-10-1 USPATFULL
CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:19) (9CI) (CA
INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{N} \\ \text{Cl} \\ \text{NH} \\ \text{F} \\ \text{OH} \\ \text{Me} \\ \end{array}$$

●19/10 HCl

RN 193000-26-9 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{C1} \\ \text{N} \\ \text{N} \\ \text{MeO} \\ \\ \text{NH} \\ \text{OH} \\ \\ \text{Me} \\ \end{array}$$

● HCl

● HCl

RN 193000-41-8 USPATFULL CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4quinazolinyl]amino]-4-fluoro-2-methyl-, hydrochloride (10:9) (9CI) (CA INDEX NAME)

●9/10 HCl

RN 193000-42-9 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)

•2 HCl

RN 193000-43-0 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

●9/5 HCl

RN 193000-44-1 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]-2-methyl-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

●6/5 HCl

RN 193000-45-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

RN 193000-46-3 USPATFULL CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-, hydrochloride (5:9) (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{CH}_2\text{-CH}_2\text{-O} & \text{N} \\ \text{MeO} & \text{NH} \\ \end{array}$$

●9/5 HCl

RN 193000-47-4 USPATFULL
CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]4-quinazolinyl]amino]-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

●6/5 HCl

RN 193000-59-8 USPATFULL CN Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-, hydrochloride (10:19) (9CI) (CA INDEX NAME)

●19/10 HCl

RN 193000-76-9 USPATFULL
CN Phenol, 5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2 methyl- (9CI) (CA INDEX NAME)

RN 193000-77-0 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(2-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-78-1 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-79-2 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-80-5 USPATFULL

CN Acetamide, N-[4-[[[4-[(3-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-81-6 USPATFULL

CN Phenol, 5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-82-7 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-83-8 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ N & & & \\ & & & \\ N & & \\ M & & \\ & & \\ N & & \\ O & & \\ M & & \\ \end{array}$$

RN 193000-84-9 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-85-0 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{S} \\ \end{array} \begin{array}{c} \text{CH}_2 - \text{O} \\ \text{MeO} \\ \end{array} \begin{array}{c} \text{N} \\ \text{NH} \\ \\ \text{Me} \\ \end{array}$$

$$\begin{array}{c|c} CH_2-O & N & N \\ \hline NNH & NH & OH \\ \hline Me & Me & \end{array}$$

RN 193000-87-2 USPATFULL
CN Phenol, 4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

RN 193000-88-3 USPATFULL

CN Acetamide, N-[4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]-2-thiazolyl]- (9CI) (CA INDEX NAME)

RN 193000-89-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(phenylmethoxy)-4-quinazolinyl]oxy]- (9CI) (CA INDEX NAME)

RN 193000-90-7 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[3-(4-pyridinyl)propoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{(CH}_2)_3 - \text{O} & \text{N} \\ & \text{MeO} & \text{NH} \\ & & \text{OH} \\ & & \text{Cl} \\ \end{array}$$

RN 193000-91-8 USPATFULL

CN Phenol, 4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

N— 
$$CH_2$$
—  $CH_2$ —  $OH_2$ —  $O$ 

RN 193000-92-9 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193000-93-0 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} CH_2-CH_2-O & N \\ \hline N & N \\ \hline MeO & NH \\ \hline Me & OH \\ \end{array}$$

RN 193000-94-1 USPATFULL

CN Phenol, 4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

RN 193000-96-3 USPATFULL

CN Phenol, 5-[[7-[(2-chloro-6-methyl-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{N} \\ \text{N} & \text{MeO} & \text{N} \\ \text{Cl} & \text{NH} \\ \text{F} & \text{OH} \\ \text{Me} & \text{OH} \\ \end{array}$$

RN 193000-97-4 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(4-pyridinylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ N & & & \\ & & & \\ MeO & & & \\ & & & \\ NH & & \\ & & & \\ NH & & \\ & & \\ OH & & \\ \end{array}$$

RN 193000-98-5 USPATFULL

CN Phenol, 5-[[7-[(2-chloro-4-pyridinyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{C1} \\ \text{N} \\ \text{N} \\ \text{MeO} \\ \end{array}$$

RN 193000-99-6 USPATFULL

CN Phenol, 5-[[7-[(3,4-difluorophenyl)methoxy]-6-methoxy-4-quinazolinyl]amino]-4-fluoro-2-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c} F \\ F \\ \end{array} \begin{array}{c} CH_2 - O \\ \\ MeO \\ \end{array} \begin{array}{c} N \\ NH \\ \\ Me \\ \end{array} \begin{array}{c} OH \\ \\ OH \\ \end{array}$$

RN 193001-00-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-01-3 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[(1-methyl-1H-imidazol-2-yl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-02-4 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-[2-(1H-1,2,4-triazol-1-yl)ethoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$N \longrightarrow CH_2 - CH_2 - O \longrightarrow N$$

$$N \longrightarrow NH$$

$$NH$$

$$Me$$

$$OH$$

RN 193001-03-5 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-04-6 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[2-(4-pyridinyl)ethoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

RN 193001-06-8 USPATFULL

CN Phenol, 5-[[6-methoxy-7-(3-thienylmethoxy)-4-quinazolinyl]amino]-2-methyl-(9CI) (CA INDEX NAME)

RN 193001-09-1 USPATFULL

CN Benzonitrile, 4-[[[4-[(2-fluoro-5-hydroxy-4-methylphenyl)amino]-6-methoxy-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 193001-14-8 USPATFULL

CN Phenol, 4-fluoro-2-methyl-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

RN 193001-16-0 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[7-(phenylmethoxy)-4-quinazolinyl]amino]-(9CI) (CA INDEX NAME)

RN 193001-18-2 USPATFULL

CN Phenol, 2-chloro-4-fluoro-5-[[6-methoxy-7-[(2-methyl-4-thiazolyl)methoxy]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{N} & \text{CH}_2 - \text{O} & \text{N} \\ \text{S} & \text{MeO} & \text{NH} \\ & & \text{NH} \\ & & \text{C1} \end{array}$$

RN 193001-32-0 USPATFULL

CN Phenol, 3-[[7-[2-(1H-imidazol-1-yl)ethoxy]-6-methoxy-4-quinazolinyl]amino](9CI) (CA INDEX NAME)

N 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  N  $\sim$ 

# AUTHOR Search in CAPIUS, USPatfull, USPatz, Toxcenter

Truong 10\_088854

10/18/2005

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L17 66 SEA FILE=CAPLUS ABB=ON PLU=ON MORTLOCK A?/AU
L18 8 SEA FILE=CAPLUS ABB=ON PLU=ON L16 AND L17

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PROCESSING COMPLETED FOR L27
L28 8 DUP REM L18 L27 (8 DUPLICATES REMOVED)

## ANSWERS '1-8' FROM FILE CAPLUS

=> d ibib abs hitind L28 1-8

L28 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

2005:955257 CAPLUS ACCESSION NUMBER:

Progress in the development of selective inhibitors of TITLE:

Aurora Kinases

Mortlock, Andrew A.; Keen, Nicholas AUTHOR (S):

J.; Jung, Frederic H.; Heron, Nicola M.; Foote, Kevin M.; Wilkinson, Robert W.; Green, Stephen

AstraZeneca, Macclesfield, SK10 4TG, UK CORPORATE SOURCE:

Current Topics in Medicinal Chemistry (Sharjah, United SOURCE:

Arab Emirates) (2005), 5(8), 807-821 CODEN: CTMCCL; ISSN: 1568-0266

Bentham Science Publishers Ltd.

Journal DOCUMENT TYPE: English LANGUAGE:

Errors in the mitotic process are thought to be one of the principal sources of the genetic instability that hallmarks cancer. Unsurprisingly, many of the proteins that regulate mitosis are aberrantly expressed in tumor cells when compared to their normal counterparts. These may represent a good source of targets for the development of novel anticancer agents. The Aurora kinases represent one such family of mitotic regulators. In recent years there has been intense interest in both understanding the role of the Aurora kinases in cell cycle regulation and also in developing small mol. inhibitors as potential novel anti-cancer With several companies now starting to take Aurora kinase inhibitors into clin. development, the time is right to review the medicinal chemical contribution to developing the field, in particular to review the increasingly broad range of small mol. inhibitors with activity against this kinase family.

7 (Enzymes) CC

PUBLISHER:

THERE ARE 141 CITED REFERENCES AVAILABLE FOR REFERENCE COUNT: 141

THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L28 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

2005:955256 CAPLUS ACCESSION NUMBER:

Progress in the development of selective inhibitors of TITLE:

Aurora kinases. [Erratum to document cited in

CA142:475149]

Mortlock, Andrew; Keen, Nicholas J. AUTHOR (S):

; Jung, Frederic H.; Heron, Nicola M.; Foote, Kevin

M.; Wilkinson, Robert; Green, Stephen

Cancer and Infection Research Area (CIRA), CORPORATE SOURCE:

AstraZeneca, Macclesfield, SK10 4TG, UK

Current Topics in Medicinal Chemistry (Sharjah, United SOURCE:

Arab Emirates) (2005), 5(8), 805 CODEN: CTMCCL; ISSN: 1568-0266

Bentham Science Publishers Ltd. PUBLISHER: Journal; General Review; Errata DOCUMENT TYPE:

English LANGUAGE:

A review. An erratum. 1-0 (Pharmacology) CC INDEXING IN PROGRESS

L28 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

2005:318734 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

142:475149

TITLE:

Progress in the development of selective inhibitors of

Aurora kinases

AUTHOR (S):

Mortlock, Andrew; Keen, Nicholas J.

; Jung, Frederic H.; Heron, Nicola M.; Foote, Kevin

M.; Wilkinson, Robert; Green, Stephen

CORPORATE SOURCE:

Cancer and Infection Research Area (CIRA),

AstraZeneca, Macclesfield, SK10 4TG, UK

SOURCE:

Current Topics in Medicinal Chemistry (Sharjah, United

Arab Emirates) (2005), 5(2), 199-213

CODEN: CTMCCL; ISSN: 1568-0266 Bentham Science Publishers Ltd.

PUBLISHER: DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

English

A review. Errors in the mitotic process are thought to be one of the principal sources of the genetic instability that hallmarks cancer. Unsurprisingly, many of the proteins that regulate mitosis are aberrantly expressed in tumor cells when compared to their normal counterparts. These may represent a good source of targets for the development of novel anti-cancer agents. The Aurora kinases represent one such family of mitotic regulators. In recent years there was intense interest in both understanding the role of the Aurora kinases in cell cycle regulation and also in developing small mol. inhibitors as potential novel anti-cancer drugs. With several companies now starting to take Aurora kinase inhibitors into clin. development, the time is right to review the medicinal chemical contribution to developing the field, in particular to review the increasingly broad range of small mol. inhibitors with activity against this kinase family.

1-0 (Pharmacology)

REFERENCE COUNT:

71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER:

2003:339130 CAPLUS

DOCUMENT NUMBER:

139:143528

TITLE:

Aurora B couples chromosome alignment with anaphase by targeting BubR1, Mad2, and Cenp-E to kinetochores

Ditchfield, Claire; Johnson, Victoria L.; Tighe, AUTHOR (S):

Anthony; Ellston, Rebecca; Haworth, Carolyn; Johnson,

Trevor; Mortlock, Andrew; Keen, Nicholas; Taylor, Stephen S.

CORPORATE SOURCE:

PUBLISHER:

School of Biological Sciences, University of

Manchester, Manchester, M13 9PT, UK

SOURCE:

Journal of Cell Biology (2003), 161(2), 267-280

CODEN: JCLBA3; ISSN: 0021-9525 Rockefeller University Press

DOCUMENT TYPE:

Journal LANGUAGE: English

The Aurora/Ipl1 family of protein kinases plays multiple roles in mitosis and cytokinesis. Here, we describe ZM447439, a novel selective Aurora kinase inhibitor. Cells treated with ZM447439 progress through interphase, enter mitosis normally, and assemble bipolar spindles. However, chromosome alignment, segregation, and cytokinesis all fail. Despite the presence of maloriented chromosomes, ZM447439-treated cells exit mitosis with normal kinetics, indicating that the spindle checkpoint is compromised. Indeed, ZM447439 prevents mitotic arrest after exposure to paclitaxel. RNA interference expts. suggest that these phenotypes are due to inhibition of Aurora B, not Aurora A or some other kinase. In the absence of Aurora B function, kinetochore localization of the spindle checkpoint components BubR1, Mad2, and Cenp-E is diminished. Furthermore, inhibition of Aurora B kinase activity prevents the rebinding of BubR1 to metaphase kinetochores after a reduction in centromeric tension. Aurora B kinase activity is also required for phosphorylation of BubR1 on entry into mitosis. Finally, we show that BubR1 is not only required for spindle checkpoint function, but is also required for chromosome alignment. Together, these results suggest that by targeting checkpoint proteins to kinetochores, Aurora B couples chromosome alignment with anaphase onset.

CC 1-6 (Pharmacology)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2001:228867 CAPLUS

DOCUMENT NUMBER: 134:266318

TITLE: Preparation of quinazolines as aurora 2 kinase

inhibitors

INVENTOR(S): Mortlock, Andrew Austen; Keen, Nicholas

John

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 208 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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OTHER S	OURCE	(S):			MAR	PAT	134:	2663	18									

OTHER SOURCE(S): MARPAT 134:26631

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$$R^{2}$$
 $R^{3}$ 
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Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR6; R6 = H or alkyl; AB R5 = (un)substituted 6-membered aromatic ring containing at least one N; R1-R4

independently halo, CN, NO2, alkylsulfanyl, N(OH)R7, or R9X1; R7 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un) substituted NHCO, CONH, SO2NH, NHSO2, or NH; R9 = H or (un) substituted hydrocarbyl, heterocyclyl, or alkoxy; and at least one of R2 or R3 is other than H; or a salt, ester, amide, or prodrug thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, 2-(N-benzoylamino)-5-aminopyrimidine and 4-chloro-6,7-dimethoxyquinazoline were coupled in i-PrOH to yield II (58%). The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration of 0.00785  $\mu M$ . In addition, II gave 50% inhibition of MCF-7 cell proliferation at 1.7  $\mu M$  and reduced BrdU incorporation into cellular DNA by 50% at 1.92-2.848  $\mu M$ .

IC ICM C07D239-94

ICS C07D401-12; C07D403-12; A61K031-517; A61P035-00

28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

II

L28 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6

ACCESSION NUMBER:

2001:228866 CAPLUS

DOCUMENT NUMBER:

134:266317

TITLE:

Preparation of quinazolines as aurora 2 kinase

inhibitors

CODEN: PIXXD2

INVENTOR(S):

Mortlock, Andrew Austen; Keen, Nicholas

John; Jung, Frederic Henri; Brewster, Andrew

2

PATENT ASSIGNEE(S):

Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE:

PCT Int. Appl., 306 pp.

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

English

PATENT INFORMATION:

PATENT NO.				KIND DATE				;	APPL	ICAT	DATE						
WO	2001	0215	96		A1	-	2001	0329	1	WO 2	000-	GB35	80		2	00009	918
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      EP 1218354
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                                                            EP 2000-960840
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PRIORITY APPLN. INFO.:
                                                            GB 1999-22154
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                                                            GB 1999-22170
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                                                            WO 2000-GB3580
                                                                                            20000918
OTHER SOURCE(S):
                                  MARPAT 134:266317
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GΙ

Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR12; R12 = H or AB alkyl; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R13, or R15X1; R13 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, CO2, S, SO, SO2, or (un) substituted NHCO, CONH, SO2NH, NHSO2, or NH; R15 = H or (un) substituted hydrocarbyl, heterocyclyl, or alkoxy; R5 = NHCO2R9, NHCOR9, NHSO2R9, COR9, CO2R9, SOR9, SO2OR9, CONR10R11, SONR10R11, or SO2NR10R11; R9-R11 = independently H or (un) substituted hydrocarbyl or heterocyclyl; or R10 and R11 together with the N to which they are attached = (un) substituted heterocyclyl; R6 = H or (un) substituted hydrocarbyl or heterocyclyl; R7 and R8 = independently H, halo, alkyl, (di)alkoxy(methyl), alkanoyl, CF3, CN, NHY2, alkenyl, alkynyl, or (un) substituted Ph, PhCH2, or heterocyclyl; or a salt, ester, or amide

II

thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, a 7-step sequence involving (1) alkylation of morpholine with 1-bromo-3-chloropropane (49%), (2) addition of Et vanillate to yield Et 3-methoxy-4-(3-morpholinopropoxy)benzoate (100%), (3) nitration (86%), (4) reduction to the amine using 10% Pd/C (100%), (5) cycloaddn. with formamide to form the quinazoline (68%), (6) chlorination to give 4-chloro-6-methoxy-7-(3-morpholinopropoxy)quinazoline (60%), and (7) amination with N-benzoyl-4-aminoaniline (58%) yielded II. The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration

of

 $0.0193~\mu M.$  In addition, II gave 50% inhibition of MCF-7 cell proliferation at 1.06  $\mu M$  and reduced BrdU incorporation into cellular DNA by 50% at 0.159-0.209  $\mu M.$ 

IC ICM C07D239-94

ICS A61K031-517; A61P035-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

REFERENCE COUNT:

11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2001:228865 CAPLUS

DOCUMENT NUMBER:

134:266316

TITLE:

Preparation of quinazoline derivatives, method of preparation and use in inhibiting aurora 2 kinase

INVENTOR(S):

Mortlock, Andrew Austen; Keen, Nicholas

John

PATENT ASSIGNEE(S):

Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.		KIND DATE APPLICATION NO.									DATE					
WO 2001	0215	 95		A1 20010329					WO 2	 000-		20000918					
W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
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EP 1218	218357			A1	A1 20020703				EP 2	000-:		20000918					
EP 1218	357			В1		2005	0406										
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EE 2002	EE 200200148			Α	:	2003	0415		EE 2	002-		20000918					
AT 2926	28			E	20050415				AT 2	000-		20000918					
ZA 2002	0018	31		Α	;	2003	0605		ZA 2	002-	1831			20020305			
NO 2002	0013	95		Α		2002	0515		NO 2	002-	1395			2	0020	320	

BG 106535 A 20021229 BG 2002-106535 20020320 PRIORITY APPLN. INFO.: GB 1999-22173 A 19990921 WO 2000-GB3562 W 20000918

OTHER SOURCE(S): MARPAT 134:266316

GΙ

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

I or a salt, ester, amide or prodrug thereof, a method for the preparation of I AR and the use of the claimed compds. for inhibiting aurora 2 kinase are claimed. These compds. are useful in the treatment of cancer. In I: X is O, or S, S(O) or S(O)2 or NR10 where R10 is H or C1-6 alkyl. R5 is OR11, NR12R13 or SR11 where R11, R12 and R13 are independently optionally substituted hydrocarbyl or optionally substituted heterocyclic groups, and R12 and R13 may addnl. form together with the N atom to which they are attached, an optionally substituted aromatic or nonarom. heterocyclic ring which may contain further heteroatoms. R6 and R7 are independently H or hydrocarbyl. R8 and R9 are independently H, halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkoxymethyl, di(C1-4alkoxy)methyl, C1-4 alkanoyl, trifluoromethyl, cyano, amino, C2-5 alkenyl, C2-5 alkynyl, a Ph group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or nonarom. and may be saturated (linked via a ring C or N atom) or unsatd. (linked via a ring C atom), and which Ph, benzyl or heterocyclic group may bear on one or more ring C atoms up to 5 substituents selected from hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C2-4 alkanoyl, C1-4 alkanoylamino, C1-4 alkoxycarbonyl, C1-4 alkylthio, C1-4 alkylsulfinyl, C1-4 alkylsulfonyl, carbamoyl, N-C1-4alkylcarbamoyl, N,N-di(C1-4alkyl)carbamoyl, aminosulfonyl, N-C1-4alkylaminosulfonyl, N,N-di(C1-4alkyl)aminosulfonyl, C1-4 alkylsulfonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halo, C1-3 alkyl, C1-3 alkoxy, C1-3 alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C1-4alkoxycarbonyl. R1, R2, R3, R4 are independently halo, cyano, nitro, C1-3 alkylthio, -N(OH)R14 (R14 is H, or C1-3 alkyl), or R16X1- (X1 represents a direct bond, -O-, -CH2-, -OC(0)-, -C(0)-, -S-, -SO-, -SO2-, -NR17C(0)-, -C(0)NR18-, -SO2NR19-, -NR20SO2- or -NR21- (R17, R18, R19, R20 and R21 each independently represents H, C1-3 alkyl or C1-3alkoxyC2-3alkyl), and R16 is H, optionally substituted hydrocarbyl, optionally substituted heterocyclyl or optionally substituted alkoxy). A method for preparing I comprises reacting II where X, R8 and R9 are as defined above, R1', R2', R3', R4' are groups R1, R2, R3, R4 as defined above resp., or precursors thereof; and R85 is a leaving group, with HCR6:CR7C(O)R5', where R6 and R7 are as defined above, R5' is a group R5 as defined above or a precursor group therefore; and thereafter if desired or necessary, converting any precursor groups R1', R2', R3', R4' or R5' to groups R1, R2, R3, R4 or R5 resp., or changing a group R5 to a different such group. The compds. of the invention inhibit the serine/threonine kinase activity of the aurora 2 kinase and thus inhibit the cell cycle and cell proliferation. Procedures for assessing these properties are described and test results are given for (E)-4-[4-(2-(3-methylcyclohexylaminocarbonyl)ethenyl)anilino]-6,7dimethoxyquinazoline.

IC ICM C07D239-94

ICS A61K031-517; A61P035-00

28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS 2 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 2001:228864 CAPLUS

DOCUMENT NUMBER:

134:252355

TITLE:

Preparation of quinazolines as aurora 2 kinase

inhibitors

INVENTOR(S):

Mortlock, Andrew Austen; Keen, Nicholas

John

PATENT ASSIGNEE(S):

Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE:

PCT Int. Appl., 101 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT	NO.			KIND DATE				APPL	ICAT		DATE					
WO	2001	0215	94		A1		2001	0329		WO 2	000-	GB35	56		2	0000	918
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OTHER SOURCE(S): MARPAT 134:252355

GI

AΒ Title compds. (I) [wherein X = O, S, SO, SO2, NH, or NR8; R8 = H or alkyl; Ra = (un) substituted 3-quinolinyl or Ph; R1-R4 = independently halo, CN, NO2, alkylsulfanyl, N(OH)R12, or R14X1; R12 = H or alkyl; X1 = a direct bond, O, CH2, OC(O), CO, S, SO, SO2, or (un) substituted NHCO, CONH, SO2NH, NHSO2, or NH; R14 = H or (un)substituted hydrocarbyl, heterocyclyl, or alkoxy; or a salt, ester, or amide thereof] were prepared as aurora 2 kinase inhibitors for the treatment of proliferative diseases, such as cancer. For example, 4-phenoxyaniline HCl and 4-chloro-6-methoxy-7-(3morpholinopropoxy) quinazoline were refluxed in i-PrOH to yield II (86%). The latter inhibited the serine/threonine kinase activity of aurora 2 kinase by 50% at a concentration of 0.069  $\mu M$ . In addition, II gave 50% inhibition of MCF-7 cell proliferation at 2.89  $\mu M$  and reduced BrdU incorporation into cellular DNA by 50% at 3.68  $\mu M$ .

II

IC

ICM C07D239-94 ICS C07D401-12; A61P035-00; A61K031-517

28-16 (Heterocyclic Compounds (More Than One Hetero Atom)) CC Section cross-reference(s): 1

I

REFERENCE COUNT:

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT Truong 10 088854

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L9

L10

(FILE 'HOME' ENTERED AT 12:29:46 ON 18 OCT 2005)

FILE 'REGISTRY' ENTERED AT 12:30:01 ON 18 OCT 2005 D SAV

ACT TRU854STRA/A

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L1STR

5754 SEA SSS FUL L1 L2

STRUCTURE UPLOADED L3 50 SEA SUB=L2 SSS SAM L3 L4D SCA

FILE 'STNGUIDE' ENTERED AT 12:31:59 ON 18 OCT 2005

FILE 'REGISTRY' ENTERED AT 13:18:48 ON 18 OCT 2005

STRUCTURE UPLOADED L5

50 SEA SUB=L2 SSS SAM L5  $_{
m L6}$ D SCA

FILE 'STNGUIDE' ENTERED AT 13:20:02 ON 18 OCT 2005

FILE 'STNGUIDE' ENTERED AT 13:23:09 ON 18 OCT 2005

FILE 'CAPLUS' ENTERED AT 13:25:02 ON 18 OCT 2005 L716 SEA ABB=ON PLU=ON L6

FILE 'REGISTRY' ENTERED AT 13:25:49 ON 18 OCT 2005 3987 SEA SUB=L2 SSS FUL L5 L8 SAVE L8 TRU854STRG/A

FILE 'CAPLUS' ENTERED AT 13:26:43 ON 18 OCT 2005

FILE 'STNGUIDE' ENTERED AT 13:27:12 ON 18 OCT 2005

FILE 'REGISTRY' ENTERED AT 13:27:35 ON 18 OCT 2005

FILE 'STNGUIDE' ENTERED AT 13:28:21 ON 18 OCT 2005

FILE 'REGISTRY' ENTERED AT 14:23:59 ON 18 OCT 2005 STRUCTURE UPLOADED O SEA SUB=L8 SSS SAM L9

FILE 'STNGUIDE' ENTERED AT 14:25:15 ON 18 OCT 2005

FILE 'REGISTRY' ENTERED AT 14:27:20 ON 18 OCT 2005 STRUCTURE UPLOADED

L11 26 SEA SUB=L8 SSS SAM L11 L12 D SCA

FILE 'STNGUIDE' ENTERED AT 14:29:12 ON 18 OCT 2005

FILE 'CAPLUS' ENTERED AT 14:33:19 ON 18 OCT 2005 26 SEA ABB=ON PLU=ON L12 L13

FILE 'REGISTRY' ENTERED AT 14:34:10 ON 18 OCT 2005 89 SEA SUB=L8 SSS FUL L9 L14

## SAVE L14 TRU854STRH/A

L17 L18	296 SEA ABB=ON PLU=ON KEEN N?/AU 66 SEA ABB=ON PLU=ON MORTLOCK A?/AU 8 SEA ABB=ON PLU=ON L16 AND L17 7 SEA ABB=ON PLU=ON L15 NOT L18 0 SEA ABB=ON PLU=ON L19 AND L16
L22	FILE 'REGISTRY' ENTERED AT 14:42:46 ON 18 OCT 2005  ANALYZE PLU=ON L14 1- LC: 5 TERMS  D
L23	FILE 'USPATFULL, USPAT2, TOXCENTER' ENTERED AT 14:45:14 ON 18 OCT 2005 14 SEA ABB=ON PLU=ON L14
	FILE 'REGISTRY' ENTERED AT 14:45:34 ON 18 OCT 2005
	FILE 'CAPLUS' ENTERED AT 14:45:37 ON 18 OCT 2005 D STAT QUE L15
	FILE 'USPATFULL, USPAT2, TOXCENTER' ENTERED AT 14:48:22 ON 18 OCT 2005 D STAT QUE NOS L23
	FILE 'CAPLUS, USPATFULL, USPAT2, TOXCENTER' ENTERED AT 14:50:13 ON 18 OCT 2005
L24	
	FILE 'STNGUIDE' ENTERED AT 14:52:34 ON 18 OCT 2005
L25 L26 L27	25 SEA ABB=ON PLU=ON MORTLOCK A?/AU
	FILE 'CAPLUS' ENTERED AT 14:54:59 ON 18 OCT 2005 D QUE L18
	FILE 'USPATFULL, USPAT2, TOXCENTER' ENTERED AT 14:55:26 ON 18 OCT 2005 D QUE L27
L28	FILE 'CAPLUS, TOXCENTER' ENTERED AT 14:55:50 ON 18 OCT 2005 8 DUP REM L18 L27 (8 DUPLICATES REMOVED) ANSWERS '1-8' FROM FILE CAPLUS

FILE 'STNGUIDE' ENTERED AT 14:57:21 ON 18 OCT 2005

D IBIB ABS HITIND L28 1-8

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.  $\,$ 

STRUCTURE FILE UPDATES: 17 OCT 2005 HIGHEST RN 865410-76-0 DICTIONARY FILE UPDATES: 17 OCT 2005 HIGHEST RN 865410-76-0

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FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 14, 2005 (20051014/UP).

FILE CAPLUS

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FILE COVERS 1907 - 18 Oct 2005 VOL 143 ISS 17 FILE LAST UPDATED: 17 Oct 2005 (20051017/ED)

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FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 Oct 2005 (20051018/PD)
FILE LAST UPDATED: 18 Oct 2005 (20051018/ED)
HIGHEST GRANTED PATENT NUMBER: US6957446
HIGHEST APPLICATION PUBLICATION NUMBER: US2005229280

CA INDEXING IS CURRENT THROUGH 18 Oct 2005 (20051018/UPCA) ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Oct 2005 (20051018/PD) REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

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>>> USPAT2 is now available. USPATFULL contains full text of the
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>>> original, i.e., the earliest published granted patents or
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    applications. USPAT2 contains full text of the latest US
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>>> publications, starting in 2001, for the inventions covered in
>>> USPATFULL. A USPATFULL record contains not only the original
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>>> publications. The publication number, patent kind code, and
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>>> the earliest to the latest publication.
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#### FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 18 Oct 2005 (20051018/PD)
FILE LAST UPDATED: 18 Oct 2005 (20051018/ED)
HIGHEST GRANTED PATENT NUMBER: US2004187682
HIGHEST APPLICATION PUBLICATION NUMBER: US2005229256
CA INDEXING IS CURRENT THROUGH 18 Oct 2005 (20051018/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Oct 2005 (20051018/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

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### FILE TOXCENTER

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